EXHIBIT B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO WAVE 5**	**Master File No. 2:12-MD-02327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

EXPERT REPORT OF BRUCE ROSENZWEIG, M.D.

I. BACKGROUND AND QUALIFICATIONS

I am currently an Assistant Professor of Obstetrics and Gynecology at Rush University Medical Center in Chicago, Illinois. My Curriculum Vitae more fully reflects my training, background, and publications. I received my MD degree in 1984 from the University of Michigan in Ann Arbor, Michigan. Following graduation from medical school, I completed an Obstetrics and Gynecology Residency at Michael Reese Hospital in Chicago. In 1988, I attended a one year pelvic surgery fellowship at State University of New York in Syracuse, New York. Following that fellowship, I attended a two year Urogynecology and Urodynamics fellowship at UCLA Harbor General Hospital in Torrance, California. After graduating from the Urogynecology fellowship, I became a faculty member at the University of Illinois in Chicago. I started a Urogynecology program at the University of Illinois and also was the residency program director. In 1998, I went into private practice, and subsequently established a private practice at Rush University Medical Center. I have also worked at John H. Stroger Hospital here in Chicago from May 2003 until November 2010 and Weiss Memorial

Hospital as Associate Chair of Gynecology from February 2011 until July 2012. I have published numerous articles and given numerous lectures on the topics of pelvic organ prolapse, urinary incontinence and repair of pelvic organ prolapse.

Throughout my career, I have performed over a thousand pelvic floor surgical procedures, including abdominal sacrocolpopexy, uterosacral suspensions, sacrospinous ligament fixations, native tissue repairs, biological graft repairs and synthetic mesh repairs. I have also used numerous synthetic pelvic mesh products, including Ethicon's TVT, TVT Obturator, and Prolift. In addition, I have performed over 300 surgeries dealing with complications related to synthetic mesh, including the removal of numerous TVT devices. I was also invited by Ethicon and attended both its Gynecare Prolift Training Seminar and TVT Obturator Seminar in Belgium. In addition, I was also invited and attended a Bard Avaulta training seminar.

A true and correct copy of my CV and Fee Schedule is attached as Exhibit "A." A list of my recent trial testimony is attached as Exhibit "B." A list of the materials I reviewed for this report is attached as Exhibit "C," in addition to any documents identified throughout this report.

II. SUMMARY OF OPINIONS

In formulating my opinions and preparing this report, I reviewed scientific literature, corporate documents from Ethicon, sample products and depositions of Ethicon employees. The corporate documents, sample products and depositions were supplied to me by counsel. All opinions I have are to a reasonable degree of medical and scientific certainty. I understand discovery is still ongoing in this case, and I reserve my right to amend my opinions if further information is provided in any form including, but not limited to corporate

documents, depositions and the expert reports of both Plaintiff and Defense experts.

My expert opinions can be summarized as follows:[1]

A. Ethicon's old construction mesh (Prolene), used in the TVT-Secur, is not suitable for its intended application and not reasonably safe as a permanent prosthetic implant for stress urinary incontinence because it is too rigid or stiff, the pores are too small, it is heavyweight mesh, it degrades over time, and causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, biofilm formation and infections.

B. Laser cutting a mesh as small as the TVT-S increased the rigidity or stiffness of the mesh.

C. The risks of degradation, chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, biofilm formation and infections were foreseeable risks of harm posed by the mesh, which could have been reduced or avoided by the adoption of the reasonable alternative designs and procedures set forth in this and my prior report.

D. Ethicon knew that the old construction (Prolene) was not appropriate for use in its TVT-S device but has failed to modify/change the laser cut mesh to a larger pore, lighter weight, less rigid mesh that would not increase the risk of erosions and sexual dysfunction, degrade, cause excessive foreign body reactions, and cause excessive shrinkage/contraction because of its economic interest in maintaining its competitive advantage in the mid-urethral ("MUS") market and, therefore, Ethicon put profits before patient safety.

E. Ethicon's warnings and disclosures of adverse events in its TVT-S Instructions for Use ("IFU") have been inadequate based on the adverse reactions and risks associated with the TVT-S that have been known to Ethicon from the time the TVT (the TVT-S' predicate device and foundation for the TVT-S' IFU) was first sold and marketed.

F. Ethicon did not disclose information to physicians in its IFUs regarding characteristics of the old construction mesh (Prolene) that makes it unsuitable for its intended application as a permanent prosthetic implant for stress urinary incontinence, including that it is too rigid, small pore,

[1] This is not intended to be an exhaustive recitation of my opinions in this case. The full scope of my opinions are described in further detail in this report, previous deposition testimony, and previous reports on this device.

heavyweight mesh, it degrades over time, and causes chronic foreign body reactions, fibrotic bridging, and mesh contracture/shrinkage.

G. The foreseeable risks of harm mentioned above could have been reduced or avoided by providing reasonable instructions or warnings as set forth in my prior report.

H. Ethicon did not inform physicians and patients that Material Safety Data Sheets ("MSDS") for polypropylene resin used to manufacture polypropylene meshes warned against use of the mesh in a permanently implanted medical device as it is incompatible with peroxides and that studies showed that it caused sarcomas in laboratory rats.

I. Ethicon did not properly inform physicians that toxicity testing of the polypropylene mesh revealed that it was cytotoxic.

J. Ethicon's promotional materials sent to physicians related to the TVT- S were inaccurate and failed to reveal material information promoted in the materials about complications/risks and conflict of interests regarding data.

K. Ethicon's collection and reporting of adverse events and complications to physicians and patients is misleading, inaccurate and incomplete.

L. The benefits of the TVT-S are outweighed by the severe, debilitating and life changing complications associated with the TVT-S.

M. For a number of reasons, the TVT-S was poorly designed and was a defective product/medical device. For instance, the TVT-S is more prone to failing and not maintaining the angle of correction at the urethra for control of stress incontinence because the length of the tape and the mechanism of insertion were different from the TVT and TVT-O. The TVT-S also had inadequate fixation and lack of support within the first 12 weeks because of the use of Ethisorb, tape length, and the release mechanism that were all known to affect the anchoring of the TVT-S. Such problems were known to Ethicon and also explained the inferior cure rates Ethicon saw with the TVT-S as compared to its predicate devices. Surgeons, particularly those who had implanted TVTs and TVT-Os, were unaware that additional tension was necessary to implant the TVT-S, resulting in lower cure rates and greater risk of mesh erosion/extrusion. Further, the arrowhead inserter was more likely to cause injury upon insertion and removal.

N. Ethicon recognized the difficulty of the surgical technique employed to implant the TVT-S and that surgeons with less skill would most likely have greater rates of mesh complications/failures. As such, Ethicon should not have marketed the TVT-S to all doctors. Ethicon failed to properly recruit, train, and monitor surgeons who were convinced by

sales representatives that the TVT-S was superior to its predicate devices because it was "less invasive."

O. Ethicon failed to adequately test the design features of the TVT Secur.

III. BACKGROUND AND TREATMENT OPTIONS FOR SUI

A. STRESS URINARY INCONTINENCE ("SUI")

Approximately one of three women over 45 years old has some form of urinary incontinence. The majority of those women do not seek medical advice or treatment for a variety of reasons.

In a continent individual, increased abdominal pressure is evenly distributed over the bladder, bladder neck, and urethra. The urethral sphincter is thus able to withstand this pressure and maintain continence. In a person with pure stress urinary incontinence (SUI), either the urethra is hypermobile or the sphincter is intrinsically deficient. In urethral hypermobility, the urethrovesical junction (UVJ) is displaced extra-abdominally, and the increased intra-abdominal pressure is unevenly distributed such that the sphincter can no longer withstand the pressure and urine leaks. With intrinsic sphincter deficiency (ISD), the UVJ is not hypermobile; however, the maximal urethral closing pressure, the Valsalva leak-point pressure, or both are too low to withstand the increase in intra-abdominal pressure and, thus, urine leaks past the sphincter.

SUI is the involuntary leakage of urine during moments of physical activity that increases abdominal pressure, such as coughing, sneezing, laughing, or exercise, in the absence of a bladder contraction. It has been estimated that 14% of women have SUI. SUI is a common type of urinary incontinence in women. Urodynamic proven SUI is found in approximately 50% of women presenting for evaluation of urinary incontinence. Symptomatic women with SUI have social or hygienic consequence from their urine loss. SUI can happen

when pelvic tissues and muscles, which support the bladder and urethra, become weak and allow the bladder "neck" (where the bladder and urethra intersect) to descend during bursts of physical activity (urethral hypermobility). This descent can prevent the urethra from working properly to control the flow of urine. SUI can also occur when the sphincter muscle that controls the urethra weakens (intrinsic sphincter deficiency). The weakened sphincter muscle is not able to stop the flow of urine under normal circumstances, and when there is an increase in abdominal pressure. Weakness may occur from pregnancy, childbirth, aging, or prior pelvic surgery. It has been estimated that a majority of incontinent women have a combination of urethral hypermobility and ISD. Other risk factors for SUI include chronic coughing or straining, constipation, obesity and smoking. Finally occult or latent SUI is defined as a positive stress test, loss of urine with increased intra-abdominal pressure and between 350-450cc volume in the bladder, after the repositioning of pelvic organ prolapse (usually accomplished with a ring pessary carefully positioned as to avoid compression of the urethra) in an otherwise clinically continent patient.

B. NONSURGICAL TREATMENT OF SUI

There are numerous non-surgical treatments available to women with SUI. First, Pelvic Floor Exercises which is a type of exercise to strengthen the pelvic floor by contracting and relaxing the levator muscles that surround the opening of the urethra, vagina, and rectum. These exercises, commonly referred to as Kegel exercises, improve the pelvic floor muscles' strength and function. Kegel exercises can improve overactive bladders by increasing urethral resistance with can trigger the bladder to relax.

Second, Pessary: A removable device that is inserted into the vagina against the vaginal wall and urethra to support the bladder neck. This helps reposition the urethra to reduce SUI.

These can be made of rubber, latex or silicon. Inserted into the vagina, a pessary rests against the back of the pubic bone and supports the bladder. Pessaries are available in various forms, including donut and cube shapes, and must be fitted by a healthcare provider. Some women who have stress incontinence use a pessary just during activities that are likely to cause urine leakage, such as jogging. Special incontinence pessaries have a 'knob,' which fits under the urethra to elevate the midurethral to prevent urine loss.

Third, Transurethral Bulking Agents: Bulking agent injections are applied around the urethra that make the space around the urethra thicker, thus helping to control urine leakage. The effects are usually not permanent.

Fourth, Behavioral Modification: This includes avoiding activities that trigger episodes of leaking. Lifestyle modification can improve stress incontinence symptoms and include quitting smoking, weight loss, and allergy treatment during seasonal allergies.

Fifth, Urinary seals: These are adhesive foam pads, which women place over the urethral opening. The pad creates a seal and prevents the leakage of urine, providing incontinence treatment. The pad is removed before urination and replaced with a new one afterward. The pad can be worn during exercise or physical activity, but not during sexual intercourse.

Sixth, Urethral insert: A thin, flexible tube that is solid rather than hollow (like a catheter) is placed into the urethra to block the leakage of urine. These small plugs are inserted into the urethra by women to prevent leakage, and are removed prior to urination. These inserts can be uncomfortable and may increase the risk of urinary tract infection.

Seventh, Bladder neck support device: This device is a flexible ring with two ridges. Once inserted into the vagina, the ridges press against the vaginal walls and support the

urethra. By lifting the bladder neck, it provides better bladder control in women suffering from stress incontinence. The device needs to be sized to fit, and must be removed and cleaned after urination. Bladder neck support devices can be uncomfortable and may cause urinary tract infections.

C. SURGICAL TREATMENT OF SUI

1. THE BURCH COLPOSUSPENSION

Retropubic approaches for the treatment of stress urinary incontinence include the Burch retropubic urethropexy (both open and laparoscopic) and the Marshall-Marchetti-Krantz (MMK) procedure. The goal of both of these procedures is to suspend and stabilize the urethra so that the urethrovesical junction (UVJ) and proximal urethra are replaced intra-abdominally and to recreate a firm backstop for intra-abdominal pressure. This anatomic placement allows normal pressure transmission during periods of increased intra-abdominal pressure restoring continence in a previously incontinent, hypermobile UVJ.

The Burch procedure was described in 1961. Initially, Burch described attaching the paravaginal fascia to the arcus tendineus. However, this was later changed to Cooper's ligaments because these were felt to provide more secure fixation points, and less chance of infection as seen with the prior MMK procedure.

Patients with type III stress urinary incontinence (a fixed, nonfunctioning proximal urethra) are not ideal candidates for a Burch procedure as no hypermobility exists to correct. For the Burch procedure, a low Pfannestiel incision is made above the pubic bone in order to enter the space of Retzius (the anatomical space between the pubic bone and the bladder above the peritonium in order to suspend the bladder and/or to perform a paravaginal repair. The procedure involves

placing permanent stitches adjacent to the neck of the bladder and either proximal or distal to the bladder neck stitches on each side and suturing them Cooper's ligament which is attached to the pubic bone. The paravaginal repair is very similar except that the stitches are attached to the arcus tendentious linea pelvis. The likelihood of success of the Burch and the paravaginal repair procedures is reported to be 80-90% in most cases. Success means total elimination of the incontinence and patient satisfaction score greater than 90%. Improved means significant reduction of urine loss and greater than 70% improvement of patient satisfaction scores. Additionally, these retropubic procedures can be accomplished by the laparoscopic route. With respect to the selection of synthetic absorbable suture versus non-absorbable suture, and braided versus monofilament, no prospective randomized blinded data exist to suggest superiority of one suture material over another. However, recognized risks are associated with bone anchors. Modifications in the technique can be used if co-existent central defect cystocele is present and obliteration of the cul-de-sac can be performed to prevent enterocele or posterior vaginal wall prolapse after Burch colposuspension.

2. PUBOVAGINAL SLING PROCEDURES

Pubovaginal slings have excelled overall success and durable cure. The procedure involves placing a band of autologous, allograft, xenograft or synthetic material directly under the bladder neck (ie, proximal urethra) or mid-urethra, which acts as a physical support to prevent bladder neck and urethral descent during physical activity. This is brought up through the rectus fascia. The sling also may augment the resting urethral closure pressure with increases in intra-abdominal pressure.

Historically, surgeons have used the fascia lata sling for recurrent SUI after a failed anti- incontinence operation. Furthermore, this operation is used extensively for the treatment

of primary ISD. If the abdominal tissues are weak and attenuated or if the vaginal tissues are atrophied or in short supply, constructing a pubovaginal sling from the leg fascia lata can be performed. This procedure is more involved than the creation of the rectus fascial sling as it requires a second incision to harvest the fascia lata and healing in an area remote for the index procedure.

An alternative to a long rectus sling is construction of a short sling from a much smaller piece of abdominal fascia (rectus fascia suburethral sling). The surgical procedure is similar to that used for the rectus fascia pubovaginal sling, except that the harvested fascial tissue is much smaller and the operation time shorter. The advantage of this procedure is its simplicity. No extensive dissection in the suprapubic area is necessary, and the postoperative result is similar to that of the full-length fascial strip sling.

An alternative to a long fascia lata sling is the use of a postage stamp–sized patch of fascia lata from the outer thigh (fascia lata suburethral sling). The surgical procedure is similar to that for the fascia lata pubovaginal sling, except the harvested fascia is much smaller. This operation does not require extensive dissection in the thigh area, and the postoperative result is similar to that of the full-length fascia lata strip sling. Postoperative convalescence is shorter than that of the fascia lata pubovaginal sling procedure.

The vaginal wall suburethral sling helps restore urethral resistance by increasing urethral compression and improving mucosal coaptation of the bladder neck. This operation is attractive because it is simple and easy to perform. Postoperative complications are minimal, and the recuperative period is short. Vaginal sling surgery is relatively contraindicated in elderly women with atrophic vaginitis. If recognized before surgery, the atrophied vaginal wall may be revitalized with the administration of vaginal estrogen cream or tablets for 3-6

months.

A clear contraindication to pubovaginal sling surgery is pure urge incontinence or mixed urinary incontinence (MUI) in which urge is the predominant component. An inherent risk of any sling procedure is de novo or worsening urge symptoms; thus, surgeons must identify and treat the presence of an urge component before surgery.

Conversely, poor detrusor function is a relative contraindication to pubovaginal sling surgery because the potential for urinary retention is increased. Women with absent or poor detrusor function in the presence of SUI are at a higher risk of experiencing prolonged postoperative urinary retention.

3. MIDURETHRAL SYNTHETIC SLINGS

Based on the "Integral theory of female incontinence," Prof. Ulmsten developed a midurethral procedure to treat stress urinary incontinence. The first reports of this procedure appeared in 1996 as an intravaginal slingoplasty. The "tape'" was placed through a small vaginal incision at the midurethra, brought through the urogenital diaphragm through the retropubic space and exited through small suprapubic incisions. The operation was theorized to correct incontinence by recreating the midurethral support of the pubourethral ligament and also by creating a midurethral hammock for support of the urethra during stress events. The procedure was described to have a success rate of 85-90% with an additional 5-10% significantly improved. The Gynecare TVT system was introduced in the US in November of 1998. Early studies showed that the risk of bladder perforation during the procedure occurred in 5-10% of cases and vascular injury with hematoma formation occurring in 2-5% of patients.

In an attempt to decrease the risk of bladder perforation and vascular injury, a "top- down" approach to trocar placement was promoted as the SPARC procedure, introduced in the US in

2001 by American Medical Systems (AMS). The next modification of the midurethral sling came in 2001 when Delorme described his results for the use of the obturator membrane and inner thigh for passage of the sling material. The proposed advantage was avoidance of the retropubic space, thus avoiding bladder perforation and retropubic vascular injury. The trocars were passed from the inner thigh through the obturator membrane from an "outside – in direction."

The next modification came from de Leval in 2003, with the "inside-out" trocar placement for the transobturator sling. This modification came around 2006 with the release of the mini-slings, or single incision slings, which use support devices at the ends of shorter mesh lengths to accomplish fixation without the need for a secondary cutaneous exit point. The mini- slings could be placed in a retropubic or "U" fashion or a hammock or "H" fashion.

IV. EXPERT OPINIONS

A. ETHICON'S PROLENE MESH WAS NOT SUITABLE FOR ITS INTENDED APPLICATION.

Polypropylene mesh (Prolene), the same mesh used in the TVT-S, has many characteristics that make it unsuitable for use as a product intended for permanent implantation in the human vaginal floor. These characteristics include the following: (1) excessive rigidity of laser-cut mesh; (2) degradation of the mesh; (3) chronic foreign body reaction; (4) infections and bio-films; (5) fibrotic bridging leading to scar plate formation and mesh encapsulation; and (6) shrinkage/contraction of the encapsulated mesh.

As a result of these and other inadequacies with the mesh, and for the reasons set forth below, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT-S causes a multitude of injuries, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain,

recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for

additional surgeries, among others. As a result, Ethicon's TVT-S (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

1. LASER-CUT MESH

The Prolene mesh in the TVT-S is laser-cut in the manufacturing process, as opposed to being mechanically cut.[2] This means that the plastic mesh is cut into strips using a laser instead of a cutting blade.[3] The result is that the mesh itself is stiffer than mechanically cut mesh.[4]Internally, Ethicon noted that laser cut mesh "was about three times stiffer than the machine-cut TVT mesh."[5] However, Ethicon decided against conducting clinical testing to establish the safety and efficacy of the devices affected by using the laser cut mesh.[6] In fact, the difference in the stretch profile between mechanically cut and laser-cut mesh led Carl G. Nilsson and Christian Falconer, two of the inventors of the original TVT,[7] and Jean de Leval, the inventor of TVT-O refused to use and questioned the use of laser-cut mesh.[8] Moreover, according to the J&J Defendants, use of the laser-cut mesh would make them unable to rely on the original studies and data they use to tout the safety and effectiveness of the original

[2] ETH.MESH.03941617; Deposition of Dan Smith, May 15, 2014, 48:11-17.
[3] Deposition of Dan Lamont, September 11, 2013, 12:13-13:14.
[4] ETH.MESH.01809080-01809081.
[5] ETH.MESH.01809080-ETH.MESH.01809081.
[6] ETH.MESH.01221735-ETH.MESH.01221740.
[7] Ulmsten U, Falconer C, Johnson P, Jomaa M, Lanner L, Nilsson CG, et al. A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. Int J Urogynecol J Pelvic Floor Dysfunct 1998;9:210 –3.
[8] ETH.MESH.16416002-16416004; ETH.MESH.04048515-0404852; ETH.MESH.03941617.

TVT.[9] Even though, laser-cut mesh was never assessed on its own in a clinical trial.[10] Finally, the rigidity of the laser-cut mesh can cause a higher incidence of erosion and sexual dysfunction than mechanically cut mesh.[11]

The difference in the stretch profile between mechanically cut and laser cut mesh also led Carl G. Nilsson and Christian Falconer, two of the inventors of the original TVT,[12] and Jean de Leval, the inventor of TVT-O, to refuse to use, and question the use, of laser cut mesh.[13] Moreover,

according to the J&J Defendants, use of the laser cut mesh would make them unable to rely on the original studies and data they use to tout the safety and effectiveness of the original TVT.[14] Additionally, laser cut mesh was never assessed on its own in a clinical trial.[15] Ethicon's Medical Director, Piet Hinoul, even noted in 2011, after the launch of the TVT Exact, that there was is no literature that allows him to discriminate which clinical trials have used laser cut versus mechanical cut.[16] [17]

Based on my experience, training, review of the literature, and review of Ethicon's internal documents, the laser cut mesh in the TVT Exact is defective because it is too stiff and rigid. As a result, the mesh increases complications including chronic pain, chronic dyspareunia, erosions, and urinary dysfunction.

---

[9] ETH.MESH.06040171-06040173.
[10] ETH.MESH.03941617.
[11] ETH.MESH.00294195-00294203; ETH.MESH.00271641; ETH.MESH.00328895; ETH.MESH.03916716.
[12] Ulmsten U, Falconer C, Johnson P, Jomaa M, Lanner L, Nilsson CG, et al. A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. Int J Urogynecol J Pelvic Floor Dysfunct 1998;9:210 –3.
[13] ETH.MESH.16416002-16416004; ETH.MESH.04048515-04048520.
[14] ETH.MESH.06040171-06040173.
[15] ETH.MESH.03941617.
[16] ETH.MESH.00576844.
[17] Notably, Dr. Hinoul's trial testimony in *Batiste v. Ethicon*, is in direct contradiction to his statement in this email that all of the TVT-Os tested in his study were laser cut. Presumably in order to convince the doctor to use the TVT Exact.

2. THE PROLENE MESH IN TVT-S DEGRADES OVER TIME

The mesh used in the TVT-S was originally designed in 1974 for use in the abdomen for treatment of hernias, and it has not changed since then.[18] Ethicon describes this mesh as the "old, old" mesh: "The first generation (old, old) mesh is utilized currently in the TVT product…."[19] The current Material Specifications for TVT-S Mesh list it as: "Old Construction PROLENE* Mesh."[20] Dan Smith testified that even when the original hernia mesh was updated for use in the abdomen, Ethicon continued to use the "old, old" mesh for TVT-S and does to this day, as follows:

> Q: So TVT kept the old when hernia changed to the new.
>
> A: Also known as original, yes.
> Q: The mesh that was used in the TVT-R is called sometimes by Ethicon indocuments old construction or original mesh; correct?
> A: Yes. Yes.[21]

In the late 90's, Ethicon determined that, in the hernia applications, it was safer to move to a lighter weight, larger pore mesh. Ethicon made a similar determination for meshes to be used in the pelvic floor.[22] However, Ethicon never updated the "old, old" hernia mesh used in the TVT-S.[23] Notably, in my opinion this makes science and information regarding hernia meshes and other pelvic meshes of particular relevance when discussing the TVT-S mesh as Ethicon chose to move to large pore, lighter weight meshes in these areas; however, not for the TVT-S.

The placement of permanent polypropylene mesh in the human vagina creates

[18] Smith Dep. (2/3/2014) 723:9-724:6.
[19] Smith Dep. (2/3/2014) 723:9-724:6.
[20] ETH.MESH.10633520 at 3522.
[21] Smith Dep. (2/3/2014) 723:9-724:6.
[22] *See, e.g.*, ETH.MESH.07455220 (discussing mesh shrinkage/contracture and stating: "Since this phenomenon occurs most frequently in small pore, heavy weight mesh, ETHICON has developed large pore, light weight meshes, i.e. GYNECARE GYNEMESH PS Nonabsorbable Prolene Soft Mesh….").
[23] Smith Dep. (2/3/14) 829:16-829:19.

problems because of the chemical composition and structure of the mesh and the physiological conditions of the vagina and the surrounding tissues. There have been numerous studies over the last 30 years which have shown polypropylene to be chemically reactive and not inert, with flaking and fissuring demonstrated by scanning electron microscopy, which leads to degradation and release of toxic compounds into pelvic tissues. This process enhances the inflammatory and fibrotic reactions within the tissues in the pelvic floor, causing a multitude of problems.[24] There have been studies suggesting that oxidation of the mesh occurs because of the polypropylene and the conditions in which it is placed.[25] The oxidation causes the mesh to degrade, crack and break apart.[26] In a recent study, 100 pelvic mesh implants were compared and over 20% showed degradation to mesh fibers.[27]

Because of the structural complexities of the vagina and the nature of the chemicals ordinarily found in the vagina and its surrounding tissues**,** there are several reasons why polypropylene presents unique problems when placed in the vagina. An Engineering Bulletin from Propex, entitled "*EB-405, The Durability of Polypropylene Geotextiles for Waste Containment Application*," from 2011, states that, "[P]olypropylene is vulnerable to the following substances: highly oxidized substances such as (peroxide), certain chlorinated hydrocarbons (halogenated hydrocarbons), and certain aromatic hydrocarbons."[28] It is well known to physicians with expertise in the pelvic floor that vaginal and perivaginal tissues are ready

[24] [18] Coda A., *Hernia 2003*;7:29; Jongebloed, WL, "*Degradation of Polypropylene in the Human Eye: A SEM Study*,"
Doc. Ophthalmol., 1986 64(1:143-152); Skrypunch, O.W., "*Giant Papillary Conjunctivitis from an Exposed Prolene Suture*," Can. J Ophthalmology, 198621:(5: 189-192).
[25] Costello C., *et al.*, "*Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants from a Single Patient*," Surgical Innovation , 2007, 143:168- 176).
[26] *Id.*
[27] Clavé A, Yahi H, Hammou JC, Montanari S, Gounon P, Clavé H, "*Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants,"* J Biomed Mater Res B Appl Biomater, 2007, Oct 83(1:44-9).
[28] *Citing* Schneider H., *Long Term Performance of Polypropylene Geosynthetics, "Durability and Aging of Geosynthetics, Koerner*, RM, Ed., (Elsevier 1989) 95-109.

sources for peroxide. The vaginal species lactobacillus produces hydrogen peroxide and lactic acid from collagen that is produced in the squamous cells of the vagina. Estrogen is the catalyst for the production of collagen from the vaginal cells. It is also well known that hydrogen peroxide produced by the lactobacillus species is important in controlling the vaginal micro- flora.

In fact, the vagina is a ready source of hydrogen peroxide production. In a manuscript from M. Strus, "*The In Vitro Effects of Hydrogen Peroxide on Vaginal Microbial Communities*," the authors show the amount of hydrogen peroxide produced by the lactobacillus species.[29] "Hydrogen Peroxide reached concentrations of from 0.05 to 1.0 mm, which under intensive aeration increases even up to 1.8 mm."[30] These results confirmed the previous results of M. Strus in the publication, "*Hydrogen Peroxide Produced by Lactobacillus Species as a Regulatory Molecule for Vaginal Micro-flora*," Med Dosw Mikrobiol, 2004: 56 (1:67-77).

It is also known that aromatic hydrocarbons can be found in the human body. In a paper from HB Moon entitled, "*Occurrence and Accumulation Patterns of Polycyclic Aromatic Hydrocarbons and Synthetic Musk Compounds in Adipose Tissues of Korean Females*," *Chemosphere* 2012 (86:485-490), these aromatic hydrocarbons were noted to be present in, "[t]otal concentrations of PAHs and SMCs in adipose tissues rang[ing] from 15 to 361 (mean:119) ngg(-1) lipid weight and from 38 to 253 (mean:106) nng(-1) lipid weight respectively…. The results of this study provide baseline information on exposure of PAHs and SMCs to the general population in Koreans."

---

[29] Strus, M., et al., *The In Vitro Effect of Hydrgen Peroxide in Vaginal Microbial Communities*, FEMS Immunol Med
Microbiol, 2006 Oct; 48(1:56-63).
[30] *Id.*

It has also been determined that halogenated hydrocarbons can be found not only in adipose tissue but also the blood stream. A paper entitled, "*Determination of Volatile Purgeable Halogenated Hydrocarbon in Human Adipose Tissue and Blood Stream*," from the *Bulletin of Environmental Contamination and Toxicology*, Volume 23, Issue 1, pp 244 – 249 published in 1979, found halogenated hydrocarbons, pesticide by-products, both in human adipose tissues and the blood stream. In a subsequent paper from 1985 in *Environmental Health Perspectives*, Volume 60, pp. 127-131, Henry Anderson, in his paper entitled, "*Utilization of Adipose Tissue Biopsy and Characterizing Human Halogenated Hydrocarbon Exposure*," also found these pesticide by-products in human adipose tissue. Accordingly, the body location where the polypropylene mesh is being placed can expose it to known chemical degradation agents.

However, chemical degradation is not the only way that polypropylene degrades *in vivo*. In a paper from N Das in the Journal of Biotechnology Research International, Volume 2011, Article ID 941810, entitled, "*Review Article: Microbial Degradation of Petroleum Hydrocarbons Contaminant: An Overview*," found that various bacteria such as Pseudomonas species, Bacillus species, Mycobacterium and Corynebacterium species, which are present in a woman's vagina, can degrade petroleum hydrocarbons. Also fungi such as the Candida species, also present, can degrade petroleum-based hydrocarbons.[31] Microbial agents that can be found inside the normal and abnormal flora of the human vagina such as Candida and, with certain pelvic infections such as Bacillus and Pseudomonas, can be a source of biological degradation of polypropylene products.

A paper entitled, "*Health, Safety and Environment Fact Sheet: Hazardous Substances - Plastics*," from CAW/TCA (www.caw.ca), August 2011:343, found that polypropylene

[31] Das, N , et al., *Review Article: Microbial Degradadtion of Petroleum Hydrocarbon Contaminants: an Overview*, J Biotech Res Intl, 2011, Article ID 941810, 1-13.

degradation products and residues can form carbon monoxide, acrolein, aldehydes and acids, qualifying these health hazards as toxic and irritants. In a paper from D Lithner in 2011 at 4, entitled, "*Environmental and Health Hazards of Chemicals in Plastic Polymers and Products*,"

University of Gothenburg, it is stated that, "[n]on-biodegradable polymers can be degraded by heat, oxidation, light, ionic radiation, hydrolysis and mechanical shear, and by pollutants such as carbon monoxide, sulphur dioxide, nitrogen oxide and ozone. This causes the polymer to get brittle, to fragment into small pieces and to release degradation products." (Citations omitted.) Lithner continues, "[o]ther substances (besides monomers) are often needed for polymerization to occur, for instance initiators, catalysts, and, depending on manufacturing process, solvents may also be used. The resulting plastic polymer can be blended with different additives, for instance plasticizers, flame retardants, heat stabilizers, antioxidants, light stabilizers, lubricants, acid scavengers, antimicrobial agents, anti-static agents, pigments, blowing agents and fillers, and is finally processed into a plastic product. There are many different plastic polymers and several thousand different additives, which result in an extremely large variation in chemical composition of plastic products." *Id.* at 6 (citations omitted). "Since plastic products are composed of many different chemicals, and the main part of these [are] broken down into something completely different; this complicates the prediction." *Id.* at 8. "The type and quantity of degradation products formed may also be influenced by degradation mechanisms, presence of polymerization impurities, and surrounding factors, e.g. temperature and oxygen." *Id.* at 9. "Few studies combining leaching tests with toxicity tests have been performed on plastic products." *Id.* at 12. The available peer-reviewed literature regarding degradation/oxidation of polypropylene in the human body

dates back to the 1960's and has been reported in numerous such publications.[32]

Two of the more important and salient articles regarding reported degradation in explanted surgical meshes (hernia and pelvic floor) are the Costello and Clave articles. Inhis paper, "*Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Implants from a Single Patient*," Prof. C Costello reported that hernia mesh made of polypropylene oxidized and degraded as a result of the metabolites produced by phagocytic cells during the body's inflammatory reaction to the mesh. High-magnification photographs showed cracking and peeling of the polypropylene fibers. Ethicon referenced this article in internal emails.[33]

Another article by A Clave, "*Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants*," also displayed high magnification photos of polypropylene fibers from explanted meshes and, in this case, the meshes were explanted from women's pelvic floor tissue.[34] The heavyweight meshes showed even greater cracking than the lower density meshes, but according to Prof/Dr. Clave, ALL 84 of the polypropylene explants examined showed degradation. Oxidation of the implanted mesh due to free radical attack through the synthesis of peroxides, superoxides and hypochlorous acid during the chronic inflammatory phase was listed as just one potential cause for the oxidative degradation within the "septic environment" in which the pelvic meshes are placed.

Given the information available to Ethicon in the scientific and medical literature concerning the potential for degradation of polypropylene, it is my opinion to a reasonable degree of

---

[32] Liebert, T, et al., *Subcutaneous Implants of Polypropylene Filaments*, J Biomed Mater Res. 1976 (10:939-951); Williams, D., *Review of Biodegradation of Surgical Polymers*, J Materials Sci, 1982 (17:1233-1246); Oswald, H.J., et al., The Deterioration of Polypropylene By Oxidative Degradation, Polymer Eng Sci, 1965 (5:152-158).

[33] ETH.MESH.005588123.

[34] Clave, A., *Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants*, I Urogynecol J 2010 21:261-270.

medical certainty that Ethicon should have conducted clinically relevant testing to determine if naturally occurring conditions in the vagina could cause polypropylene to degrade and if so, what the quantity and quality of the products of degradation would be, whether they would be released into surrounding tissues and/or migrate in the woman's body, what the clinical implications for the woman would be and whether some women's body's would react differently to the mesh and degradative process and its by-products.

Ethicon's Daniel Burkley, a Principal Scientist at Ethicon, testified that the science supported the conclusion that mesh could shrink, contract and degrade. Specifically, Mr. Burkley agreed that the risk of degradation increases when you have a severe inflammatory response with mesh implanted in a contaminated field.[35] Mr. Burkley also testified that polypropylene mesh in human beings is subject to some slight degree of surface degradation.[36]He agreed that degradation might be better understood if Ethicon studied or tested a product that is permanently implanted in women.[37] In fact, according to Mr. Burkley, Ethicon only conducted one study related to degradation and Prolene material. This study consisted of a Prolene suture implanted into dogs.[38] Mr. Burkley testified that the study and photos from the dog actually showed that the Prolene material used in TVT ABBREVO degraded and was still degrading after 7 years.[39]

It is now clear from Ethicon's internal documents that Mr. Burkley was incorrect when he said that Ethicon only performed one study related to degradation of Prolene. Contrary to Mr. Burkley's claim, he and other Ethicon scientists were involved in a Prolene human explant study that was conducted in 1987 which found that Prolene degrades while in the body.

[35] Burkley Dep. (5/22/13) 184:17-24.
[36] Burkley Dep. (5/22/13) 206:2-11
[37] Burkley Dep. (5/22/13) 206:12-25.
[38] ETH.MESH.05453719 (Seven year data for ten year Prolene study: ERF 85-219).
[39] Burkley Dep. (5/23/13) 315:8-13.

According to Ethicon's documents, Ethicon's scientists received 58 Prolene human explants from Professor Robert Guidon[40] which were analyzed by Ethicon's scientists using scanning electron microscopy ("SEM"). The SEM study revealed that 34 of the 58 Prolene explants (58%) were cracked. Further studies, including FTIR and melt point analysis, were conducted by Ethicon's scientists to determine the cause of the cracking observed in Professor Guidon's explants. In a report authored by Mr. Burkley on September 30, 1987, he concluded that the Prolene explants had insufficient antioxidants to protect them from oxidation which led to *in vivo* degradation of the Prolene devices.[41] Importantly, Ethicon has not made any changes to Prolene since it was introduced to the market, except that, in 2011, they reduced the amount of Sanatanox (another antioxidant), which could potentially make Prolene more, not less, susceptible to oxidized degradation.[42] Thus, Ethicon's internal studies clearly demonstrate that Ethicon's scientists had concluded that Prolene can degrade while implanted in the human body.

Ethicon subsequently hired an outside consulting firm to resolve the cause of the erosion of its surgical meshes for the pelvic floor. In a June 22, 2011 report, PA Consulting Group informed Ethicon that, "[p]olypropylene can suffer from degradation following implant… a process which initiates after a few days post implantation in animal studies."[43] The consulting report discusses numerous images of polypropylene mesh that show "physical degradation" of the mesh.[44] In addition, in a 2009 presentation, Ethicon Medical Director Piet

[40] DEPO.ETH.MESH.00004755
[41] ETH.MESH.12831391 at ETH.MESH.1281392
[42] ETH.MESH.02589032 and ETH.MESH.07192929 (May 18, 2011 PA Consulting Report: Investigating Mesh Erosion in Pelvic Floor Repair and PowerPoint presentations
[43] ETH.MESH.02589032 and ETH.MESH.07192929 (May 18, 2011 PA Consulting Report: Investigating Mesh Erosion in Pelvic Floor Repair and PowerPoint presentation).
[44] *Id.*

Hinoul stated that meshes are not biologically inert.[45]

I have personally seen mesh that is broken, cracked and looks different from when it was in the package. Interestingly, despite years of scientific literature, its own internal dog study and reports from consultants it hired that concluded that the degradation of mesh occurs, Ethicon's Instructions for Use (IFU) continues to claim to this day that the mesh in the TVT-S, "is not absorbed, nor is it subject to degradation or weakening by the action of enzymes."[46] This is not simply inaccurate, but is false and misleading for all of the reasons stated above, including, most importantly, that Ethicon's own internal documents and testimony from its employees confirm that the mesh degrades.

It is my opinion to a reasonable degree of medical certainty that the mesh used in TVT-S degrades. The effect of chemical and biological degradation of the TVT-S Prolene mesh in a woman's tissues can lead to a greater foreign body reaction, enhanced inflammatory response and excessive scarring, which can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT-S mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

Given the information available in the scientific and medical literature concerning the

[45] ETH.MESH.01264260 (Presentation, "Prolift+M," P Hinoul, MD, Ethicon Pelvic Floor Expert's Meeting – Nederland, Utrecht, May 7, 2009).
[46] ETH.MESH.02340568-ETH.MESH.02340590.

potential for degradation of polypropylene, it is my opinion to a reasonable degree of medical certainty that Ethicon should have conducted clinically relevant testing to determine if naturally occurring conditions in the vagina could cause polypropylene to degrade and if so, what the quantity and quality of the products of degradation would be, whether they would be released into surrounding tissues and/or migrate in the woman's body, what the clinical implications for the woman would be and whether some women's body's would react differently to the mesh and the degradative process and its by-products.

Moreover, Ethicon failed to inform physicians or patients about the potential for degradation of the mesh and the complications that could follow. In fact, Ethicon not only failed to disclose these risks to physicians and patients, it did not accurately describe these significant risks by calling them "transitory" and by putting inaccurate statements about degradation in its IFU. This is information physicians need to know in order to have a fair and proper conversation with their patients about the use of a product. Physicians rely on device manufacturers to inform them of the risks and complications associated with its products instead of downplaying them or inaccurately stating them. By not disclosing this safety information to physicians and their patients, it is my opinion to a reasonable degree of medical certainty that Ethicon failed to properly inform physicians and patients about the risks of degradation of Prolene mesh in the TVT-S. In addition, by failing to inform physicians, Ethicon did not provide them with an opportunity to discuss these risks with their patients.

3. CHRONIC FOREIGN BODY REACTION

The human body has a natural and fairly predictable "host defense response" to any foreign object placed inside of it. Whether a splinter or a surgical mesh, the human body will send white blood cells to attack the invader and, if the products of inflammation cannot ward off or

destroy the invader, including if the invader is anything from bacteria to prosthetic implants, the initial acute inflammatory phase is followed by a chronic inflammatory phase. Therefore, with the placement of something like a permanent surgical mesh in human tissues, there will be a chronic or permanent foreign body reaction to the implant, as well as a chronic inflammatory response by the body.[47] In fact, Ethicon Medical Directors, Piet Hinoul and Charlotte Owens, have both testified that the chronic foreign body reaction created by the body's response to mesh can cause a severe inflammatory reaction, which can cause chronic pain, nerve entrapment, erosions, dyspareunia and the need for additional surgeries.[48]

Other consultants and experts in the field informed Ethicon that there would be chronic tissue reaction to its polypropylene meshes. During a 2006 meeting at one of Ethicon's facilities, Bernd Klosterhalfen, a pathology consultant expert for Ethicon, informed Ethicon that there can be a continuing reaction between tissues in the body and mesh for up to 20 years.[49] In addition, during a February 2007 meeting, Ethicon stated that there can be, "[E]xcessive FBR [foreign body reaction]> massive scar plate > more shrinkage."[50]

Internally, Ethicon's scientists agreed. Dr. Holste testified that chronic foreign body reactions occurs in Ethicon's small pore, heavyweight meshes like the Prolene mesh found in TVT-S.[51] In fact, Dr. Holste testified that Ethicon developed lighter weight, large pore meshes in order to minimize the complications seen with heavyweight meshes like the Prolene used

[47] Klinge, U., et al., *Shrinking of Polypropylene Mesh In Vivo: An Experimental Study in Dogs*, Eur J Surg 1998, 164: 965-969; Klinge, U., *Foreign Body reaction to Meshes Used for the Repair of Abdominal Wall Hernias*,Eur J Surg 1998, 164:951–960; Klostherhalfen,B., *The lightweight and large porous mesh concept for hernia repair*, Expert Rev. Med. Devices 2005, 2(1); Binnebosel M, et al., *Biocompatibility of prosthetic meshes in abdominal surgery*, Semin Immunopathol 2011, 33:235-243; ETH.MESH.03658577 (Biocompatibility of Ultrapro).
[48] Hinoul Dep. (4/5/12) 99:09-25; (4/6/12) 518:14-520:20; (6/26/13) 175:1-176:17;184:18-22; 328:10-24; Owens Dep. (9/12/2012) 98:11-99:07.
[49] ETH.MESH.00870466 (June 6, 2006 Ethicon Expert Meeting Meshes for Pelvic Floor Repair, Norderstedt).
[50] ETH.MESH.01218361 (Ethicon Presentation: "State of Knowledge in 'mesh shrinkage'-What do we know").
[51] Holste Dep. (7/29/13) 52:5-55:21.

in TVT-S.[52] Ethicon employee, Christophe Vailhe, testified that there can be an excessive inflammatory reaction or foreign body reaction that would lead to mesh erosion and contraction.[53] Despite its knowledge about the problems associated with chronic foreign body reaction, Ethicon continues to use a heavyweight, small pore mesh in its TVT-S product.

Contrary to this scientific evidence, Ethicon informed doctors in its IFU that its TVT-S mesh was "non-reactive with a minimal and transient foreign body reaction."[54] This was despite all of the internal documents and testimony discussed above from Ethicon's Medical Affairs and Research and Development employees that chronic foreign body reaction occurs in small pore, heavyweight meshes like the Prolene mesh in TVT-S. Moreover, as one of Ethicon's lead engineers stated: "the foreign body reaction is not transitory – it doesn't ever go away, but decreases over time to a minimal level."[55] That is, it is chronic. I have reviewed numerous pathology reports from my own patients and other physician's patients and pathology reports reviewed in litigations describing foreign body reactions. Hence, the mesh potentiates a chronic, long-term inflammation. This is contrary to the express language of the TVT-S IFU and, to this date, has yet to be corrected in that IFU.

For the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT-S creates a chronic foreign body reaction which can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of

[52] Holste Dep. (7/29/13) 51:3-53:6.
[53] Vailhe Dep. (6/21/13) 383:8-19.
[54] ETH.MESH.02340829.
[55] ETH.MESH.00211259.

the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

Moreover, Ethicon failed to inform physicians or patients about the potential for a severe, chronic foreign body response and the complications that could follow. In fact, not only did Ethicon fail to disclose these risks, it mischaracterized the risks by calling them "transitory" and by putting inaccurate statements about foreign body response in its IFU. This is information physicians need to know in order to have a fair and proper conversation with their patients about the use of a product. Physicians rely on device manufacturers to inform them of the risks and complications associated with its products instead of downplaying them or inaccurately stating them. By not disclosing this safety information to physicians and their patients, it is my opinion to a reasonable degree of medical certainty that Ethicon failed to properly inform physicians and patients about the risks of foreign body response of Prolene mesh in the TVT-S. In addition, by failing to inform physicians, Ethicon did not provide them with an opportunity to discuss these risks with their patients.

4. INFECTIONS/BIO-FILMS

The placement of midurethral slings, including TVT-S, violates one of the most basic tenets of surgical teachings in that it is the placement of a permanent implant into the human through a "clean contaminated" surgical field, *i.e.* the vagina, which is not sterile and can never be completely sterilized, therefore, implantation through the vagina is contraindicated for every procedure and implantation.

In the TVT-S, the weave of the mesh produces very small interstices which allow bacteria to enter and to hide from the host defenses designed to eliminate them. The bacteria can secrete an encasing polysaccharide slime (biofilm), which further serves to shield the bacteria from destruction by white blood cells and macrophages.[56] The effect and consequences of biofilm is to increase the foreign body reaction, resulting in chronic infections, chronic inflammation, erosions, and mesh and scar contracture, and was well known to Ethicon, as evidenced by the testimony of Ethicon's Head of Pre-Clinical, Dr. Joerg Holste.[57]

Importantly, the biofilm actually serves as a protection for the bacteria surrounding the mesh fibers against the body's host defense response (white blood cells), which are intended to destroy foreign invaders like bacteria. Thus, the weave induces the creation of a shield against the body's defenses to the bacteria entrained in the woven mesh, inhibiting the body's ability to fight off the infective agents within the mesh. The large surface area promotes wicking of fluids and bacteria which provides a safe haven for bacteria which attach themselves to the mesh during the insertion process.[58] Daniel Burkley testified that reducing surface area could reduce the amount of chronic inflammation.[59] Additionally, the size of the mesh placed equates to a large surface area with many places for bacteria to hide while being protected from host defenses leading to numerous complications.[60]

---

[56] Osterberg, B., et al., *Effect of Suture Materials on Bacterial Survival in Infected Wounds: An Experimental Study*, Acta. Chir. Scand 1979, 145:7 431-434; Merritt, K., *Factors Influencing Bacterial Adherence to Biomaterials*, J Biomat Appl 1991, 5:185-203; An, Y., *Concise Review of Mechanisms of Bacterial Adhesion to Biomaterial Surfaces*, J Biomed Mater Res (Appl Biomat) 1998, 43:338-348; The TVM Group: J. Berrocal, et al., *Conceptual advances in the surgical management of genital prolapsed*, J Gynecol Obsted Biol Reprod 2004, 33:577-587.

[57] Holste Dep. (7/30/13) 295:24-298:14, 411:15-414:24.

[58] Klinge, U., et al., *Do Multifilament Alloplastic Meshes Increase the Infection Rate? Analysis of the Polymeric Surface, the Bacteria Adherence, and the In Vivo Consequences in a Rat Model*, J Biomed Mater Res 2002, 63:765-771; Vollebregt, A, et al., *Bacterial Colonisation of Collagen-Coated Polypropylene Vaginal Mesh: Are Additional Intraoperative Sterility Procedures Useful?*, Int Urogyn J 2009, 20:1345-51.

[59] Burkley Dep. (5/22/13) 371.

[60] Klinge, *supra* n. 26; Vollebregt, *supra* n. 26

There have been numerous peer-reviewed journal articles regarding secondary-mesh related infections as well as the dangers of implanting surgical mesh in a clean/contaminated field. Of note, in May of 2013, at the AUA meeting in San Diego, Dr. Shah and his colleagues reported on the "*Bacteriological Analysis of Explanted Transvaginal Meshes,*" which included explanted samples of both SUI slings and prolapse meshes. Of the 50 explants examined, 52% of those explanted due to patient complaints' of painful mesh were infused with pathogenic organisms, 20% of those explanted due to vaginal erosions had pathogenic organism, and 83% of those explanted due to urinary tract erosions were contaminated with pathogenic organisms.[61]

When polypropylene particles separate from the surface of the mesh fiber due to degradation, see infra, the surface area of the mesh is greatly increased thus providing even greater areas for bacterial adherence to the mesh, more elution of toxic compounds from the polypropylene, and also more of the free toxic polypropylene itself, all of which increases the inflammatory reaction and intensity of the fibrosis.[62] This cracking of the mesh surface also provides safe harbors for infectious bacteria to proliferate.

In his periodic histopathological analyses for Ethicon of its pelvic floor explants, Dr. Klosterhalfen reported to Ethicon that, in virtually 100% of those instances in which mesh had been explanted due to erosions, he found a secondary, mesh-related infection at the tissue/mesh interface.[63] Mesh exposure and erosion cause the fibers to be further exposed to bacteria that will adhere to and colonize on the mesh surface.

Ethicon employees have testified that they were aware of these biofilms forming on the surface

[61] Shah, K., et al., Bateriological Analysis of Explanted Transvaginal Meshes (Abstract 1144).
[62] Jongebloed, *supra*, n. 1; Sternschuss, G, et al., *Post-Implantation Alterations of Polypropylene in the Human*, J Urol 2012, 188:27-32; Clave, *supra*, at 6.
[63] ETH.MESH. 00006636.

of the mesh.[64] However, Ethicon never performed any long-term, clinical studies to determine whether the warnings given them through the peer-reviewed literature and by their own experts and consultants were accurate, namely that mesh-related infections are real; that they cause patient injury in the form mesh erosions and recurrent, late infections; and that the transvaginal implantation through and into the non-sterile, septic vagina is below the standard of care for any surgical technique, especially one used to treat non-life threatening conditions, such as stress urinary incontinence.

Therefore, it is my opinion to a reasonable degree of medical certainty that the TVT-S mesh is susceptible to biofilm formation due to the weave of the mesh allowing the infiltration, harboring, and protection of bacterial contaminants; the degraded mesh surface harboring bacteria; the passage through and into a clean/contaminated field; and after exposure/erosion of the mesh into the vagina or other organs, further contamination of the mesh with a multitude of vaginal flora that further increases the risk of harmful and recurrent infections in women. Accordingly, the TVT-S transvaginal technique, as well as the TVT-S mesh itself, are not safe for their intended purpose of implantation into a woman's pelvic tissues and can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT-S mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

[64] Holste Dep. (7/30/13) 283:19-284:5.

Finally, Ethicon's claims in its IFU that the TVT-S mesh may "potentiate infection" are misleading, at best. If, by the intentionally ambiguous term, "potentiate," Ethicon means "cause," then this is false for all of the reasons stated above. If by "potentiate," Ethicon means "exacerbate an existing infection," then the statement is misleading at best. Ethicon failed to warn physicians and patients that a slimy, protective biofilm could form on the mesh leading to painful erosions, recurrent, late infections and the need for mesh removal. The TVT-S IFU contrasts sharply with the PROLENE IFU on this issue. The PROLENE IFU states as follows: PROLENE Mesh in contaminated wounds should be used with the understanding that subsequent infection ma y require removal of the material.[65]

Ethicon did not to include this risk, despite that unlike hernia mesh, TVT mesh is being implanted through a contaminated environment – the vagina. By failing to include this risk, Ethicon did not adequately warn physicians about these important risks, nor by extension, provide surgeons with an opportunity to discuss these risks with their patients.

5. PORE SIZE AND FIBROTIC BRIDGING

Fibrotic bridging occurs when the fibers surrounding the pores of the mesh are too close together to allow the tissue in the pore enough room to recover from the trauma of tissue damage due to implanting a surgical prosthetic device. Pores that are large enough for good, newly- vascularized tissue tend to be filled with fatty tissue versus small pores that become filled with scarred or fibrotic tissue. In those instances, the scar forms across the pores or "bridges" from one side of the pore to the other. This can occur either due to the granulomas around the mesh fibers joining together or due to densely-formed fibroblasts between these granulomas. Either way, such bridging can lead to the creation of a rigid, scar plate that can encapsulate the mesh with scar tissue. Simply put, small mesh pores that cause fibrotic

[65] ETH.MESH.05920616 (7/20/07 Email from Chomiak, M. re Defining Light Weight Mesh).

bridging turn the mesh into a solid sheet of scar tissue and there is no space or room for tissue to grow into the mesh, which is the intended purpose of the mesh. The fibrotic bridging and scar plate prevents tissue in-growth and causes complications, including, among other things, pain with the rigid mesh, shrinkage or contraction of the mesh, erosions due to mechanical irritation in the tissue of a rigid, scar- plated mesh, nerve entrapment, chronic pain and dyspareunia.

This concept is best illustrated by a DVD produced by Ethicon which features an Ethicon consultant, Dr. Todd Heniford, talking about a heavyweight, small pore mesh called Marlex used for hernia repairs.[66] The Prolene mesh used in TVT-S is of heavyweight, small pore construction and, in fact, is even heavier than Marlex. Ethicon Scientists have acknowledged that the Marlex mesh in the video is similar to the Prolene in TVT-S in that is heavy weight small pore mesh.[67] In the video, Dr. Heniford talks about the dangers of heavy weight, small pore meshes.[68] In fact, Dr. Heniford states, "there is no excuse for using heavy weight, small pore meshes in the human body."[69]

I have explanted numerous TVT meshes and have witnessed meshes with extensive scar plating and mesh encapsulation similar to the hardened/stiffened mesh viewed in the Heniford video. In numerous emails, Ethicon employees discussed concerns regarding fibrotic bridging.[70] They have testified that the heavy weight, small pore type of mesh in the TVT-S

---

[66] Heniford, B.T., 2007, *The benefits of lightweight meshes in Ventral Hernia Repair in Ventral Hernia Repair*, Video produced by Ethicon.

[67] ETH.MESH.05918776 (5/04/04 Email from Schiaparelli, Jill, Strategic Grown Subject: Marlex Experience); Batke Dep. (8/01/13) 87:12 - 88:10, 113:3-114:3, 257:23-259:13; Holste Dep (7/29/13) 51:3-53:6, 55:22-57:4; Vailhe Dep. (6/20/13) 182:2 185:5.

[68] Heniford Video, supra, n. 46.

[69] *Id.*

[70] ETH.MESH.04037600 (Innovations in mesh development); ETH.MESH.05920616 (7/20/07 ; Emails from Chomiak, M. to Batke, B., et al. re Defining light weight mesh); ETH.MESH.05585033 (Boris Batke Presentation – Project Edelweis – Ultrapro); ETH.MESH.05446127 (3/13/2006 Emails from Holste, J. to Engel, D., et al.re Mesh and Tissue Contraction in Animal – "Shrinking Meshes?); ETH.MESH.05475773 (2/09/2007 Boris Batke, Ethicon

can lead to an increased risk of foreign body reaction, contraction of the mesh, nerve entrapment, erosions and chronic pelvic pain.[71] In other emails, when discussing these concepts, Ethicon's World Wide Marketing Director for General Surgery, Marty Chomiak, states that "… we want to avoid 'bridging', therefore we think large pores are better than small . . ."[72] Ethicon also had information and scientific knowledge regarding superior mesh designs to prevent fibrotic bridging and scar plating. Specifically, Ethicon also had scientific knowledge that light weight, large pore mesh could decrease the likelihood of foreign body reaction, fibrotic bridging and scar plating.[73]

Despite having clinical knowledge of the importance of pore size to successful outcomes, and dozens of emails about the importance of pore size, Ethicon's person most knowledgeable about pore size testified that Ethicon does not manufacture its mesh to a specific pore size. Dan Smith testified as follows:

> Q: Does Ethicon have a validated test method to determine the pore size of its TVT mesh?
> A: We determine the pore size by courses and wales and that is how it's done. So the courses and wale count is a validated test method.
> Q: And I'm talking about pore size. Does Ethicon have a validated test method to determine its pore size for its mesh?
> A: The construction of the mesh is -- does not have a pore size requirement.[74]

In fact, Ethicon does not even have a test to measure the pore size of its mesh. Dan Smith testified:

> Q. Mr. Smith, does Ethicon have a validated test to describe the pore size

---

R&D, Presentation: *The (clinical) argument of lightweight mesh in abdominal surgery*); ETH.MESH.04015102 (3/1/12 Email from Batke, Boris to Mayes, C. re AGES Pelvic Floor Conference-Gala Dinner Invitation); ETH.MESH.04037600 (3/15/12 Boris, B. PowerPoint Presentation, *Innovations in Mesh Development*, Melbourne AGES 2012).

[71] Batke Dep. (8/1/13) 87:12-88:10, 113:3-114:3, 257:23-259:13; Holste Dep. (7/29/13) 51:3-53:6, 55:22-57:4; Vailhe Dep. (6/20/13) 182:2-185:5.

[72] ETH.MESH.05920616 (7/20/07 Email from Chomiak, M. re Defining Light Weight Mesh).

[73] Batke Dep. (8/1/13) 87:12-88:10, 113:3-114:3, 257:23-259:13; Holste (7/29/13) 51:3 - 53:6, 55:22 - 57:4; Vailhe Dep. (6/20/13) 182:2-185:5.

[74] Smith Dep. (2-3-14) 729:1 to 729:12.

of its TVT meshes microns? Yes or no.
A. No….[75]

Despite the information that it did not measure pore size or manufacture its mesh to a specific requirement, Ethicon repeatedly stated in advertising and marketing materials that its mesh was "large pore." For example, in one brochure, Ethicon promotes the mesh used in the TVT family of products (including TVT-S) as the "Largest pore size" of any of its competitors, listing the size as 1379 um.[76] However, given that Ethicon has no verified methodology to measure pore size, Ethicon had no scientific basis upon which to base these statements. In fact, in internal documents, Ethicon scientists described PROLENE mesh as small pore: "Standard Mesh PROLENE small pores area weight 105 g/m2."[77] One Ethicon Engineer measured a mesh and determined that there were two pore sizes in the mesh, a "major" and "minor" pore. "There are two distinct pore sizes in the PROLENE 6 mil mesh (TVT). The major pore is about 1176 um…. The minor pore is about 295 um."[78] Certainly, neither of these pores was 1379 um, and the minor pore was substantially smaller.

In summary, for the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT-S causes fibrotic bridging in the body, resulting in an increased inflammatory response leading to a multitude of injuries, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, nerve injury, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among

[75] Smith Dep. (2-3-14) 779:5 to 779:8.
[76] ETH.MESH.00349508 at 9510.
[77] ETH.MESH.04941016.
[78] ETH.MESH.00584175 (Ex. T-3583); ETH.MESH.00584179 (Ex. T-3581).

others. As a result, the polypropylene in Ethicon's TVT-S mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

Moreover, Ethicon did not inform physicians and patients that its mesh was susceptible to fibrotic bridging. Ethicon failed to warn physicians and patients that fibrotic bridging could occur leading to painful erosions, recurrent, late infections, nerve injury and the need for mesh removal. By failing to do so, Ethicon did not adequately warn physicians about these important risks, nor by extension, provide surgeons with an opportunity to discuss these risks with their patients.

6. MESH CONTRACTURE/SHRINKAGE

Mesh contracture or shrinkage is an event that takes place after the implantation of mesh and relates to the wound healing process that occurs after the surgical trauma of implanting a foreign body made of polypropylene in the sensitive tissues of the vagina and pelvis. By 1998, polypropylene mesh was known to contract or shrink 30-50%.[79] These findings were later confirmed in numerous papers, such as those by W Cobb and his colleagues – one of whom was Dr. Henniford (referenced above).[80] This also showed that heavier weight meshes like TVT-S led to greater amounts of contraction. The works of Cobb and Klinge/Klosterhalfen have been referenced in numerous Ethicon documents. Contraction or shrinkage has been shown to draw nerves close to the midurethral sling mesh both in the transobturator application[81] and for retropubic application.[82] Furthermore, contraction or

[79] Klinge, U, *Shrinking of Polypropelen Mesh in Vivo: An Experimental Study in Dogs*, Eur J Surg 1998, 164:965-969.
[80] Cobb, W., et al., *The Argument for Lightweight Polyropylene Mesh in Hernia Repair*, Surgical Innovation 2005, 12(1):T1-T7.
[81] Corona, R., et al., *Tension-free Vaginal Tapes and Pelvic Nerve Neuropathy*, J Min Invas Gynecol 2008, 15:3

shrinkage is closely related to the pore size and weight of the mesh. Small pore, heavy weight mesh leads to fibrotic bridging which leads to scar plates, mesh encapsulation and shrinkage or contraction of the mesh, which is compounded by the shrinkage effect associated with the normal wound healing process already occurring in the tissue.

This phenomenon of shrinkage and its relation to the design of the pores as well as the consequences to the patient were illustrated in an email by Ethicon Scientist Joerge Holste in a March 13, 2006 email discussing a paper he authored entitled "Shrinking Meshes?"[83] In his email, Dr. Holste states "this was our scientific statement on mesh shrinkage: Basically, small pores, heavy weight meshes induce more fibrotic bridging tissue reaction causing more mesh shrinkage during maturation of the collagenous tissue. See my presentation about biocompatibility."[84] In addition, in a presentation by Boris Batke, Associate Director R&D, he states heavier-weight polypropylene mesh results in mesh contraction of 33%.[85] In an email dated November of 2002, related to a discussion of mesh used in a TVT product, Axel Arnaud, one of Ethicon's medical directors, used 30% shrinkage of the mesh as a "rule of thumb."[86] At an Ethicon expert meeting in Norderstedt, Germany in 2007, an Ethicon employee presented a PowerPoint entitled "Factors Related to Mesh Shrinkage" in which all of these issues were clearly laid out.[87]

Mesh shrinkage was known by Ethicon as early as 1998 in published work by Ethicon's

---

262-267; Parnell, B.A., et al.,*Genitofemoral and Perineal Neuralgia after Transobturator Midurethral Sling*, Obstet Gynecol 2012, 119:428-431; Jacquetin, B, *Complications of Vaginal Mesh: Our Experience*, Intl Urogyn J, 2009, 20:893-6; Tunn, R, *Sonomorphological Evaluation of Polypropylene Mesh Implants After Vaginal Mesh Repair in Women with Cystocele or Rectocele*, Ultrasound Obstetrics Gynecol 2007, 29:449-452.

[82] Heise, C.P., et al., *Mesh Inguinodynia: A New Clinical Syndrome After Inguinal Herniorrhaphy?*, J Am Coll Surg

[83] ETH.MESH 05446127, *supra*, n. 34.

[84] *Id*.

[85] ETH.MESH 05479717 (3/1/11 Boris Batke, Ethicon Associate Director R&D, Presentation: Ethicon Polypropylene Mesh Technology).

[86] ETH.MESH 03917375.

[87] ETH.MESH. 02017152 (Nordestadt Expert's meeting 2007); ETH.MESH.01782867 (Factors Related to Mesh Shrinking).

then consultants, Uwe Klinge and Bernd Klosterhalfen.[88] They noted in these early papers that all polypropylene meshes shrink 30-50%. This was restated in later works by W Cobb and his colleagues[89]--one of which was Dr. Heniford (referenced above). The words of Cobb and Klinge/Klosterhalfen have been referenced in numerous Ethicon documents and thus, Ethicon was well aware of these findings regarding the shrinkage or contraction of polypropylene meshes in vivo. Ethicon was further aware that heavier weight meshes led to greater amounts of contraction.

It is my opinion to a reasonable degree of medical certainty that as a result of work with internal and external experts and consultants in the late 1990s, multiple internal documents and articles, and the scientific literature as a whole, that Prolene mesh used in TVT-S not only could, but would shrink and contract, and that this shrinkage could lead to painful complications in women implanted with TVT-S, such as multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, nerve injury, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others.

As a result, the polypropylene in Ethicon's TVT-S mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to warn physicians and patients of the possibility of shrinkage and contraction and the adverse outcomes that could occur as a result.

[88] Klinge U, Klosterhalfen B, Muller M, Ottinger A, Schumpelick V. Shrinking of Polypropylene Mesh in vivo: An Experimental Study in Dogs. Eur J Surg. 1998: 164; 965-969
[89] ETH.MESH.07455220.

ETHICON FAILED TO TEST THE TVT SECUR.

A reasonable and prudent medical device manufacturer should have adequate safety data to support its products before urging surgeons to use them permanently on patients.[90] Before the Secur was launched on the market, Ethicon did not have adequate clinical data showing the TVT Exact was safe and effective. As discussed above, there was also no clinical data showing that the laser cut mesh was shown to be safe and effective. Carl Nilsson, one of the inventors of the TVT and Ethicon KOL, and Christain Falconer, another KOL, told Ethicon in early 2008 that it "is impossible and incorrect to say or assume that Laser Cut would be the same as mechanically cut. Comparative in vivo studies is a necessity to determine the differences. Theoretical calculations are not enough as evidence."[91] Despite this and the design modifications made, Ethicon chose to leverage its long term data from the TVT in order to speed the Secur to market without gathering any clinical data. This was later determined to be a cardinal sin by Ethicon.

The TVT Secur should not have reached the market without clinical studies on safety,

[90] Cornelis et al., *The introduction of mid-urethral slings: an evaluation of literature*, Int Urogynecol J (2014) "clinicians and their professional organizations should only choose devices that have adequate clinical data to support their efficacy and safety"; Abrams et al., *Synthetic Vaginal Tapes for Stress Incontinence: Proposals for Improved Regulation of New Devices in Europe*, European Urology 60 (2011) 1207-1211 "Manufacturers' responsibilities should include the following tasks: testing the device thoroughly, including carrying out appropriate clinical trials, before placing on market." "The need for randomized controlled trials (RCTs) at an early stage of development of any new device, with significant new features compared with existing tapes, was felt be essential. The clinicians expressed regret about the number of low-quality studies, usually case series, published in the literature." Kane, et al, *Midurethral Slings for Stress Urinary Incontinence*, Clinical Obst. and Gyn., Vol 5, No. 1, 124-135. ("Surgeons should be skeptical and wary of new products that lack human study data."); Deprest et al, *The need for preclinical research on pelvic floor reconstruction*, BJOG,2013. ("Often complications are caused by properties of materials that haven't been evaluated before clinical use."); Nilsson, *Creating a gold standard surgical procedure: the development and implantation of TVT*, Int. Urogyn. 2015, Dwyer, *Editorial The 75% rule: all stress incontinence procedures are alike*, Int. Urogyn. 2011; H. Azaïs et al. / European Journal of Obstetrics & Gynecology and Reproductive Biology 178 (2014) 203–207; ("Trials incorporating large amounts of patients are needed…"); Shepherd et al., *Uniaxial biomechanical properties of seven different vaginally implanted meshes for pelvic organ prolapse*, Int Urogynecol J (2012) 23:613–620 ("Despite its widespread acceptance and use, synthetic meshes have had little regulatory oversight"); Fiener et al, *Efficacy and safety of transvaginal mesh kits in the treatment of prolapse of the vaginal apex: a systemic review*, BIOG 2009;116:15-24.

[91] ETH.MESH.16416003.

efficacy, or adverse outcome data.[92] This is especially true considering the design features of the TVT Secur. It is my opinion that Ethicon failed to test the TVT Secur and mislead physicians and patients into thinking that the TVT Secur had been studied and determined to be safe and efficacious in order to drive sales of the product.

7. ETHICON HAD LIGHTER WEIGHT, LARGER PORE MESHES AVAILABLE

Ethicon did not change the Prolene mesh in its TVT device despite having better and safer options available for economic reasons. Ethicon believed that continued use of the TVT mesh gave the company an economic and competitive advantage in marketing the product because they could continue to use the existing clinical data on the product to market the device, even though because the mesh was changed, the existing clinical data would be obsolete. [93] Dr. Brigitte Hellhammer testified that despite having incorporated the use of the lightweight, large pore Ultrapro mesh in vaginal tissues for the treatment of pelvic organ prolapse, the Ultrapro was never used by Ethicon in a device used for the treatment of stress urinary incontinence largely because the company wanted to continue to rely on the Ulmsten/Nilsson series of studies on 130 patients performed with the TVT device.[94]Dr. Arnaud also confirmed that the company did not want to change anything with the mesh because of the existing clinical data on the product.[95] It is my opinion to a reasonable degree of medical certainty that Ethicon was negligent in failing to correct the defects in the TVT mesh as the company had knowledge of the defects and failed to correct the defects with products and solutions that were already available to the company because it valued its economic interests above patient

[92] Chapple, et al., *Mesh Sling in an Era of Uncertainty: Lessons Learned and the Way Forward,* J Eururo.2013.06.045.
[93] ETH.MESH.03911107
[94] Deposition of Brigette Hellhammer, MD, September 11, 2013
[95] Deposition of Axel Arnaud, July 19, 2013 36:15-37:3

safety.

B. THE TVT-S' IFU LACKED ALL KNOWN RISKS AND WAS INACCURATE.

The purpose of the IFU is for a medical device manufacturer to provide physicians with the information necessary for them to make decisions regarding the use of a medical device for a particular patient. In addition, the IFU should disclose potential adverse reactions and risks known to the medical device manufacturer to the physician so that the risks can be relayed to the patient and an informed decision regarding the use of the product can be reached. Throughout my education, training, surgical and clinical practice, I have reviewed numerous IFUs for a variety of products, including mesh products in order to understand the proper way to use the device and to gain knowledge about the complications and adverse events associated with a device. I have extensive clinical experience with IFUs and instructing patients about the adverse events/risks contained in the IFU. Similar to Medical Directors, Dr. Martin Weisberg and Dr. David Robinson, I have gained expertise in IFUs through my extensive clinical experience

reviewing IFUs, and obtaining patients' consent regarding surgeries, including Ethicon's own pelvic mesh products including the TVT line and Prolift.

Catherine Beath, Ethicon's former Vice President of Quality Assurance and Regulatory Affairs, testified that "physicians should be made aware of all the significant safety risks associated with the product in the IFU."[96] And, "a reasonably prudent medical device company would continually update the label consistent with developing data and information that becomes known to the company" when it is appropriate.[97] Similarly, former Medical Director Dr. David Robinson testified that the warnings and adverse event section of the IFU

[96] Beath Dep. (7/12/13) 592:7-11.
[97] Beath Dep. (7/11/13) 198: 8-13.

should include all significant risks and complications related to the procedure and the mesh.[98] According to Dr. Robinson, a device manufacturer must include this information because you want to make sure the doctors have all the information they need to adequately inform patients who are deciding to use the product.[99] According to Ethicon Medical Director Dr. Martin Weisberg, the goal of the IFU is to communicate the most important safety risks attributable to the TVT device and that an IFU should never exclude known hazards or complications.[100] Dr. Weisberg also believes that an IFU should not knowingly underestimate the risks of using the product.[101] And, if an IFU excludes known complications or understates the risks, it "fails in one of its principal purposes."[102]

1. THE IFU DID NOT INCLUDE ALL KNOWN RISKS

As a surgeon who has relied on dozens of IFUs to understand the risk-profile of devices and medications, it is my opinion that Ethicon did not provide physicians and patients with adequate warnings in the IFU for the TVT-S. Despite the importance of an IFU, Ethicon provided only vague potential adverse reactions. If you compare the adverse reactions/risks in the TVT-S IFUs to the adverse reactions/risks that were available and known to Ethicon at the time of the launch of TVT-S, it is clear that there are numerous adverse events absent from the IFU. For example, in the TVT-S IFU at launch, the Adverse Reactions/Risks section reads as follows:

ADVERSE REACTIONS

- Punctures or lacerations of vessels, nerves, bladder or bowel may occur during instrument passage and may require surgical repair.

[98] Robinson Dep. (9/11/13) 238:12-25.
[99] Robinson Dep. (9/11/13) 239:1-11.
[100] Weisberg Dep. (8/9/13) 659:19-660:15.
[101] *Id.* at 960:13-16.
[102] *Id*. at 961:10-17.

- Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation or inflammation.
- As with all foreign bodies and surgical implants, PROLENE Mesh may potentiate or exacerbate an existing infection.
- Over correction, i.e., too much tension applied to the tape, may cause temporary or permanent lower urinary tract obstruction.
- Under-correction or incorrect placement may result in incomplete or no relief from urinary incontinence.

Despite only listing the above adverse reactions/risks, it is clear from the testimony of Senior Ethicon Employees in both the Medical Affairs and Regulatory Affairs that every adverse reaction/risk that Ethicon has scientific knowledge of today, it had scientific knowledge about at the time the TVT was first sold and certainly in 2006 when the first TVT-S was sold, marketed and launched. Medical Director, Piet Hinoul testified that Ethicon understood the following adverse events occurred from the time the TVT was first sold, years before the first TVT-S was sold:

Erosions through vaginal epithelium
infection Pain
Urinary Problems
Erosions that could decrease patient's quality of
life Dyspareunia
Need for additional surgeries
Need for the removal of
device Urinary Tract
Infections Dysuria
DeNovo
Urgency Mesh
Exposure
Fistula
Formation
Hematoma
Abscess
Formation
Narrowing of vaginal wall
Erosion which can occur any time in future
Contracture of mesh causing pain
Complications making it impossible to have sexual
relations Worsening Incontinence

Yet, none of these were in the TVT-S IFU at launch.[103]

It was unreasonable on Ethicon's part to expect surgeons, even highly skilled ones, to know of all the potential complications of the TVT-S product and procedure simply because of their profession as doctors. In this respect, the IFU failed to warn of a number of risks associated with the use of the TVT-S to treat SUI such as mesh shrinkage/contraction, degradation of the polypropylene mesh over time, chronic pelvic pain, dyspareunia, untreatable and permanent pain, partner penile injury with intercourse, vaginal scarring, narrowing, shortening, fibrosis, scar plate formation, deformation, that the safety and effectiveness of the TVT-S had not been evaluated in either long-term clinical studies or a Randomized Control Trial ("RCT"), chronic foreign body reaction and the potential long-term consequences associated with such a foreign body reaction, the necessity of multiple surgeries to remove mesh and other complications stemming from these surgeries, that some risks were unknown due to the lack of RCTs conducted on this product, the incision size should be at least 1.5 cm, complications could appear at any time into the future and could last for the remainder of the patient's life, and the higher failure rates and reoperation rates associated with the TVT-S as compared to the TVT and TVT-O. Of course, the IFU failed to warn about the potential permanency of any of the risks in the IFU.

Indeed, Medical Director Dr. Weisberg testified that Ethicon did not include: "permanent, lifelong, worsening and debilitating pain," lifelong risk of surgical repairs for erosions, "severe or chronic inflammation," fibrotic bridging, that the product can degrade, or cause severe erosion.[104] In addition, former Medical Director, Dr. David Robinson, testified

[103] ETH.MESH.01037447 Page 6; *see also* Deposition of Charlotte Owens 6.19.13 Page 178 Line 10-14.
[104] Weisberg Dep. (8/9/13) 968:12-972:21.

that Ethicon never informed physicians that patients may require multiple surgeries to treat erosions, that erosions could be severe and untreatable, and that patients could endure lifelong severe pain or dyspareunia. This is true despite, as discussed above, Ethicon having scientific knowledge of the risks at the time of launch.

2. THE IFU INACCURATELY PORTRAYED RISKS

Internal documents show that Ethicon employees knowingly failed to disclose the TVT- S' inadequacies. When Dan Smith visited Australia, he discovered that Australian doctors were executing the procedure incorrectly. Ethicon's documents reveal that in Mr. Smith's opinion, his visit addressed concerns doctors were experiencing.[105] Communications between Dan Smith and Mark Yale, Risk Management Director, inquired whether the team is "aligned with what Dan [Smith] is communicating." Dr. Aran Maree responds that they are not "aligned" and details the differences in his response. Specifically, Dr. Maree referenced that Key Opinion Leader ("KOL") Professor Frazer reported to Dr. Maree that "the IFU is fundamentally misleading" and that "tension-free, tension-less and placement with no tension are complete misnomers."[106] Ethicon found that too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction. To the contrary, not enough tension or incorrect placement would result in incomplete or no relief from urinary incontinence.

This correspondence among other internal documents[107] outline a wide discrepancy between what Dan Smith reported back to David Robinson and others in the United States and

[105] ETH.MESH.00311792 Page 3
[106] *Id.*
[107] ETH.MESH.06051155

information Dr. Maree (in Australia) was learning from conversations with the same people.[108] Dr. Maree noted on November 2, 2007, "[i]t is my understanding that some suggestions had come out in the form of (i) increased tension required with this mesh with 'pillowing of peri-urethral tissues required,' (which is quite the opposite of TVT-O recommendations), as well as new tips and tricks to avoid dislodging the device when removing the inserters and (iii) new tips for minimal dissection when introducing the product. We also discussed the fact that at this time some or all of these suggested changes may not be incorporated into the [IFU] or technical training material."[109] Despite these known concerns with the implantation of the TVT-S and the internal turmoil within the team, Ethicon chose to never update the IFU—indeed Ethicon only had one IFU during the entire time this device was on the market. However, Ethicon chose to remedy the deficiencies of the IFU by offering "procedural pearls," "tips and tricks" and "cookbooks"—unfortunately, this information was only made available to those surgeons that chose to attend training with Ethicon.

In addition to omitting certain known risks, Ethicon significantly downplayed the risks actually listed in the IFU. This is especially true with respect to erosions. The IFU stated the risk of mesh erosion/extrusion would be immediate or "transitory." On the topic of erosions, in the Adverse Event/Risks section in the TVT-S IFU, in place from the time of launch until present day, it states:

> Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation or inflammation.

This language significantly downplays the permanent nature of erosions and suggests to physicians that erosions are a "transitory" or temporary problem. As shown in an email

[108] ETH.MESH.00311792 Page 2
[109] ETH.MESH.00312180

exchange between Ethicon's Associate Medical Director of Worldwide Customer Quality Meng Chen, M.D., Ph.D. and Bryan Lisa in the Regulatory Affairs Department, it was clear that the adverse events were not "transitory." Chen wrote, "Pardon me again, from what I see each day, these patient experiences are not 'transitory' at all."[110]

As previously noted, also noticeably absent from the Adverse Reactions section was dyspareunia and chronic pelvic pain, which were known adverse reactions according to internal Ethicon documents.[111] Dr. David Robinson, Ethicon's former Medical Director, testified that these were known adverse reactions with the TVT-S.[112] Though Dr. Robinson was aware that erosion was a possible adverse reaction to the TVT-S and that possible complications associated with the TVT-S included multiple surgeries to treat the resulting erosion, though it was not included in the IFU.[113] In addition, studies revealed that women who were implanted with the TVT-S experienced higher rates of erosion and higher rates of reoperations due to the device's failure. The IFU does not even address that there is potential difficulty removing the mesh. Thus, despite the known importance of an IFU to physicians, Ethicon provided only vague potential adverse reactions.

Ethicon also had scientific evidence that erosions could occur many years after implantation of the device. In minutes from June 22, 2001 Scientific Advisory Committee on Pelvic Floor Repair, it was a "[c]onsensus: Erosion is a risk. Erosion, possibly an infection response. Typically seen by 3 mos, usually by 6-12 mos. Can present late, 3 years. To vagina-not a good situation. To bladder, urethra or rectum-a very bad situation."[114] "There have been

[110] ETH.MESH.04093125 (1/29/09 Email between Meng Chen and Bryan Lisa).
[111] ETH.MESH.04081189-ETH.MESH.04081190 (memo noting Ethicon's IFU failed to warn its patients of the TVT risks, particularly the dangers of erosion and painful sexual activity).
[112] David Robinson Dep. at 251:7-12.
[113] Deposition of David Robinson, M.D 7.24.13, 355:16-356:8.
[114] ETH.MESH.02089392.

reports of erosions into the urethra that are not picked up until months even years after the procedure."[115]In October 2002, Medical Director Dr. Martin Weisberg was involved in an email exchange with European Science Director Axel Arnaud about downplaying risks with respect to erosions. Specifically, Dr. Arnaud suggested to Dr. Weisberg that Ethicon needed "to be more elusive" when discussing potential complications like erosions.[116]

According to Medical Director Dr. Martin Weisberg and former Medical Director Dr. David Robinson, Ethicon never disclosed or warned doctors or patients in IFUs or Patient Brochures that the use of TVT-S slings can cause lifelong risk of erosions.[117] Despite the fact Ethicon had scientific feedback from one of its own doctors that experiences were not transitory and that she had concerns about the IFU and the transitory language, Ethicon never informed physicians or disclosed it in its IFU.

In an unpublished summary of the first 12-month human data available on the TVT-S (contained in an internal Clinical Study Report) performed by 6 of the top surgeons in the world who were all Ethicon KOLs (including Vince Lucente, Mickey Karram, Walter Artibani, and Carl Nilsson), there were a total of 51 adverse events reported in 32 out of 72 patients. One of the "safety conclusions" was that "[o]nly 69.4% subjects experienced no major device-related complications."[118] This human data study went on to note "[o]nly 55% of the women reported no leak on self-assessment [the *subjective* cure rate]."[119] The summary concluded "[i]n the future, well planned randomized studies will have to be conducted in order to discern if the new single- incision procedures can achieve the same level of effectiveness as has been extensively shown with the TVT procedure and (with shorter follow-up) also with

[115] ETH.MESH.04099233 (September 24, 2008 email from Melissa Day to Meng Chen and others).
[116] ETH.MESH.03910175-03910177.
[117] Weisberg dep. (8/9/13) 968:2-969:10; Robinson Dep. (9/11/13) 329:12-330:7.
[118] ETH.MESH.02916609.
[119] ETH.MESH.02916610.

the TVT-O procedure. . . . As long as complications occur at the rate seen in this study . . . the single-incision procedure cannot be recommended as a first line treatment for [SUI]."[120]

Ethicon recognized the TVT-S was associated with significantly higher failure rates. Dr. Maree noted in an October 30, 2007 email that the rates of Dr. Lucente's failure rates of 30% as reported the update were "not at all surprising that we may have similar or higher failure rates here."[121] Dr. Maree recognized that these results were "very different to the QA database numbers sent through from the 'reported' complaint rates divided by the USA sales earlier on." *Id.*

C. ETHICON WITHHELD MATERIAL FACTS ABOUT THE TVT-S

Ethicon should have collected long-term clinical data before selling this completely different TVT product, but they chose not to collect this data. Moreover, Ethicon launched TVT- S worldwide without long-term human use data and without performing any clinical studies, including RCTs as initially promised to their KOLs. [122] They decided against it because board members wanted to accelerate the launch on the product, and performing a clinical study would have caused a delay in the product launch.[123] Furthermore, Ethicon decided against these post launch RCTs because of "budget constraints."[124]

Since the TVT was first launched, Ethicon has sent materials in various forms to physicians promoting long term follow up data on the original cohort of patients implanted with the TVT from 1995-1996.[125] Ethicon continued to cite to this data in all of various TVT

[120] ETH.MESH.02916611.
[121] ETH.MESH.03845446 Page 1.
[122] ETH.MESH.00134795.
[123] Deposition of Patricia Hojnoski April 16, 2013 Page 110 Line 15 to Page 111 Line 9.
[124] ETH.MESH.00314794 Page 4.
[125] ETH.MESH.0015598, ETH.MESH.00658058, ETH.MESH.01186068, ETH.MESH.02236784, ETH.MESH.02237103, ETH.MESH.03459211, ETH.MESH.05183409, ETH.MESH.00339437; ETH.MESH.05794787.

product materials. In addition, the materials tout low complication rates related to various adverse reactions, including erosions. These materials include press releases, marketing brochures and email blasts.

The long term data primarily relied on by Ethicon throughout these materials relates to the Ulmsten/Nilsson studies. These studies were originally started by Dr. Ulmsten, the inventor of the TVT, and continued by Dr. Nilsson after Dr. Ulmsten's death. Prior to selling the TVT to Johnson & Johnson, Dr. Ulmsten owned a company called Medscand. Johnson & Johnson hired Dr. Ulmsten and Medscand to conduct studies related to the TVT and its line of products. To this day, Ethicon relies heavily on these studies and uses them in numerous promotional materials despite the fact that Ethicon never disclosed to physicians the potential conflict of interest and inherent bias that exists due to Dr. Ulmsten's relationship with Ethicon and Johnson & Johnson. In addition, Ethicon never disclosed to physicians that the device used in the original Medscand study was different than the TVT-S device. It is important to physicians using the TVT-S that the data in these types of promotional materials is accurate, unbiased and that physicians are informed about any potential conflicts of interest in the data contained within the materials. In other words, physicians rely on Ethicon to provide fair and balanced information and to ensure that physicians have been given all the data and not just the positive press release data.

Despite using the Ulmsten data to promote the TVT-S, Ethicon never disclosed to physicians the bias and inherent conflict of interest related to the Ulmsten data. Specifically, in its promotional materials, Ethicon (Johnson and Johnson) never informed physicians about its relationship and contracts with Professor Ulmsten and his company Medscand. It is clear from the contracts that the publications and data from Dr. Ulmsten where contracted for hire

by Johnson and Johnson International.[126]

The License and Supply Agreement between Johnson and Johnson International and Medscand (Ulmsten's Company) dated February 13, 1997, states in section 3.6 Milestone Payments:

> Johnson and Johnson International (JJI) shall pay shall pay to Medscand the following payments (b). A payment in the amount of $400,000.00 due on February 28, 1997; provided, however, that in the event that Clinical Trials as specified in Exhibit C have not been completed by such date, then such amount shall not be due until the completion of the Clinical Trials.[127]

Under Exhibit F, Consulting Agreement with Professor Alf Ivar Ulmsten, section 4 Confidential Information Rights to Inventions and Copyrights (B) it states:

> Any copyrightable work whether published or unpublished created by supplier Dr. Ulmsten directly as a result of or during the performance of services herein shall be considered a work made for hire, to the fullest extent permitted by law and all rights, titles and interest herein, including worldwide copyrights shall be the property of the company as the employer and party specially commissioned said work.[128]

Finally, in Exhibit C, Clinical Trials, it states:

> The results of clinical trials will be considered acceptable if, first, they do not differ significantly from the results published in the original article published in the Int. Urogynecol J 1996-7:81-86 by U. Ulmsten, et.al., with regards to the following items: Safety 1.1, preoperative complications 1.2 , post-operative complications 1 year from operation 2. Efficacy. Second Long term results over 1 year from operation do not show a deterioration of rates significantly different from those of the standard suburethral slingplasties. It is assumed that from 12 – 60 months a gradual decrease in efficacy of 5% is normal. 3. No significant numbers of unexpected i.e. not addressed in the original article published in the Int. Urogynecol J 19967 81-86 by U.Ulmsten at et.al. procedure related i.e. not addressed in the review article published in the Int. Urogynecol J 19945: 228-239 by G. N. Ghomiem et.al. complications appear at any time in the postoperative course.[129]

In total, Dr. Ulmsten stood to gain millions of dollars for the 6 papers that he published

[126] ETH.MESH.08696085- ETH.MESH.086966134.
[127] ETH.MESH.08696091.
[128] ETH.MESH.0869116
[129] ETH.MESH.08696132.

on the TVT devices. In addition, the results of those studies would be found revenue worthy only if they did not differ from the parameters sent by Johnson & Johnson regarding complications and efficacy. The Ulmsten studies have an inherent conflict of interest and bias as they were "made for hire" and standards were set by Johnson & Johnson. As set forth above, if Dr. Ulmsten did not meet the standards set forth by Johnson & Johnson, he did not receive substantial payments for the "studies." As a result of this relationship, there is a clear conflict of interest and potential for enormous bias issues.

The conflict of interest and bias created by the relationship between Ethicon and Dr. Ulmsten was acknowledged by Dr. Axel Arnaud, Ethicon's European Medical Director, in a recent deposition. Specifically, Dr. Arnaud testified that such an agreement like the one discussed above between Dr. Ulmsten and Johnson & Johnson creates a potential conflict of interest.[130] Dr. Arnaud also acknowledged that when Johnson & Johnson enters into this type of agreement with a physician or his company and the study is published, there "certainly" needs to be a disclosure of the relationship.[131]Additionally, former Ethicon Medical Director, Dr. David Robinson, testified that in his experience working in the industry for medical device manufacturers, it is best that potential biases be disclosed.[132] He also testified that if publications from somebody like Ulmsten or Nilsson about safety and efficacy are being published, it is best if they disclose that they have a financial bias or conflict of interest.[133] In fact, in an April 2009 email exchange with Medical Director Piet Hinoul about a physician who, like Ulmsten, is a consultant and inventor for competitor Boston Scientific, Dr.

[130] Arnaud Dep. (7/20/13) 497:24-501:21, 509:8-17.
[131] Arnaud Dep. (7/20/13) 514:17-515:1.
[132] Robinson Dep. (9/11/13) 214:15-21.
[133] Robinson Dep. (9/11/12) 215:8-13.

Robinson states that that situation presents "enormous bias issues."[134] Despite two of its medical directors testifying that the relationship between Ulmsten carried over to Nilsson presents a conflict of interest and bias, Ethicon has never disclosed this information in its promotional pieces. This is information physicians and patients have a right to know so that a proper informed decision regarding the value of the data in the studies and the use of the product can be made.

Aside from never disclosing to physicians the underlying conflict of interest and bias of the Ulmsten studies in its promotional pieces, Ethicon also never informed them about other problems with the data, including incomplete data on the original cohort, data incorrectly reported and erosion rates underreported. In the original 510(k) submission for TVT Classic, Ethicon used Medscand data from the Scandinavian Multicenter Study.[135] The report shows that the 12 month follow-up was obtained for 90 of the original 131 patients, without explanation of why there was a loss of 41 patients from the study. The study also describes a complication of wound infection: "while the vaginal infection required surgical intervention with resection of exposed mesh."[136] This represents a vaginal mesh erosion/extrusion/exposure and needs to be reported as such. However, when the paper was published (Ulmsten, Int Urogynecol J 1998), the paper states that there was no defect healing and no tape rejections. It further misrepresents the outcome for this patient as "[t]he patient with the wound infection had vaginal atrophy. After minimal vaginal wall resection and effective local estrogen treatment she healed without further intervention. There was no tape rejection." *Id.*

If Ulmsten had reported a mesh erosion/extrusion/exposure with mesh excision in his study, it would not have been acceptable under Exhibit C of his consulting contract for

[134] ETH.MESH.03259439; Robinson Dep. (9/11/13) 219:6-220:10.
[135] ETH.MESH 00371587.
[136] *Id.*

payment of the $400,000.[137] This demonstrates that the results of this paper were potentially biased by the payment Ulmsten would receive for favorable data and should discount the data. At the very least, Ethicon should have informed physicians about the relationship between Ethicon and the Ulmsten studies.

Many of the marketing brochures tout the "[t]he urethral erosion rate less than or equal to that of traditional slings; no reported urethral erosions in 10 studies of 50+ patients."[138] The reference used for the first part of this statement is from Dr. Gary Leach who looked at traditional sling procedures done before 1993, when traditional slings were performed at the bladder neck and purposely placed under tension to treat severe stress urinary incontinence from intrinsic sphincter deficiency (particularly among Urogynecologists).

The second part of this statement regarding "no uretheral erosions" is incorrect. In published studies, Dr. Karram found one case of urethral erosion in his study of 350 Gynecare TVTs performed (Karram Obstet Gynecol 2003) and Hammad found nine cases of urethral erosion in his study (Hammad Eur Urol 2005).[139] His study followed the complications of 1459 patients, 993 of whom had Gynecare TVT, while the remainder had SPARC procedures. While the authors do not break down the incidence of urethral erosion by product, it is exceedingly unlikely that all erosions happen in the SPARC group. The statement regarding "no uretheral erosions" also did not include de Tayrac's 2003 paper of 61 patients (31 TVTs) which showed a 3% urethral erosion rate.[140] Dr. Shlomo Raz described a study of 26 patients who presented with voiding dysfunction, including symptoms of severe urethral, pelvic and

[137] ETH.MESH 08696132.
[138] ETH.MESH 00339439.
[139] Karram, M.M., et al., *Complications and untoward effects of the tension-free vaginal tape procedure*, Ob & Gyn 2003, 101:929-32.
[140] de Tayrac, R., et al, *A prospective randomized trial comparing tension-free vaginal tape for surgical treatment of stress urinary incontinence*, Am J Obstet Gynecol 2004, 190:602-8.

genital pain, urinary retention, recurrent UTIs, de-novo urgency with urge incontinence found to have mesh from a sling procedure in the bladder or urethra.[141] Their patients were found to have been treated conservatively with anticholinergic medication. They conclude that "dysfunctional voiding symptoms after sling procedure should elicit a high degree of suspicion if pharmacotherapy is not successful in alleviating symptoms...Cystoscopy should be considered if the patient remains symptomatic despite pharmacotherapy."

In one of the Nilsson studies, Dr. Nilsson describes four patients on "anticholinergics" (Int Urogynecol J 2008 Table 3). They conclude: "[i]t is also encouraging to see that no late adverse effects of the polypropylene tape material was found and that erosion of the tape into adjacent tissue did not occur." However, this statement cannot be made for 4 patients who are on pharmacotherapy without a cystoscopy, which was not performed in the 11 year follow-up study. Dr. Raz's review of the literature found multiple cases of urethral erosions in a large series with TVT.[142] There have also been multiple case reports attesting to the fact that urethral erosion does occur specifically with Gynecare TVT products.[143] To imply that urethral erosion does not occur is not giving physicians fair and balanced information about the true incidence of urethral erosions with TVT products.

Later, Nilsson published the 5 year follow-up of this cohort.[144] He describes the cohort: "[A] prospective open multicenter trial was conducted in the Nordic countries at the beginning

---

[141] Deng D.Y., et al., *Presentation and management of major complications of midurethral slings: Are complications under reported*, Neurourology Urodynamics 2007, 26:46-52.

[142] Karram 2003, Hammad 2005

[143] Sweat, S., *et al.*, *Polypropylene Mesh Tape for Stress Urinary Incontinence: Complication of Urethral Erosion and Outlet Obstruction*, J Urology 2002, 168:144-146; Gerstenbluth, R.E., et al, *Simultaneous Urethral Erosion of Tension-Free Vaginal Tape and Woven Polyester Pubovaginal Sling*, J Urol. 2003, (2 Pt 1) 170:525-6; Vassallo, B.J.., *et al.*, *Management of latrogenic Vaginal Constriction*, Am J Obstet Gynecol 2003, 102(3):512-20; Haferkamp, A., *et al.*, *Urethral Erosion of Tension-Free Vaginal Tape*, J Urol 2002, 167(1): 250.

[144] Ulmsten data; Nilsson, Int Urogynecol J 2001.

of 1995. The short-term results were published in 1998." This implies that these are the same patients as published in 1998. It is interesting or an incredible coincidence that the exact number of patients receiving 12 months of follow-up in the Medscand publication, ninety (90) patients was the exact number being described in the 5 year study. There is again no mention of the outcome of the other 41 patients from the original cohort. Another interesting detail in the 5 year study is that the original number of centers used for the study [six centers] was now down to 3, again without explanation. The 5 year report does describe the original patient with the wound infection but again fails to mention she had mesh excised, "1 case (1.1%) of infection of operating site was observed."

In 2006, Dr. Nilsson published a different study on the long term outcome of patients with TVT.[145] He describes his new patient population: "A multi-center study comprising only carefully selected primary cases revealed a promising cure rate of 85% after 5 years (referenced his 5 year study) and 81% at 7 years."[146] These two papers are the subject of many press releases and marketing brochures, but they never described that these were carefully selected patients. "To our knowledge, the long-term effect and effectiveness of the TVT procedure has not yet been studied in an unselected patient group. We earlier reported 16-month follow-up results of a general patient group referred to a tertiary medical unit and comprising primary, recurrent, mixed, and low pressure urethra cases. In the present study, we report the long-term results in the same above-mentioned group." They describe a 3.1% mesh "visualized" rate, half of which needed surgical resection. These results, more representative of what one would see in a normal practice, is never mentioned in press releases or marketing documents.

[145] Kuuva , N., *et al., Long-term results of the tension-free vaginal tape operation in an unselected group of 129 stress incontinent women,* Acta Obstetricia Gynecologica Scandanavica 2006, 85:4 482-87.
[146] Nilsson, Obstet Gynecol 2004.

Conversely, when Ethicon receives adverse information, it does not make it into the promotional pieces. Dr. AC Wang's abstract, "Tension-Free Vaginal Tape (TVT) for Urinary Stress Incontinence - A Preliminary Report" was used in the original 510k submission in October of 1997 as support for FDA clearance of the TVT.[147] However, when Dr. Wang reported that he had 25 cases of "failure of vaginal healing considered by him to be potential tape rejection...in each case the revision failed within 2 weeks, requiring further surgery to excise mesh and repair the vaginal wound," this important information never made it into the marketing materials or press releases.[148]

As an alternative to RCTs initially promised to certain KOLs (documents reflect they would not have endorsed the TVT-S otherwise), Ethicon started "TVT World" as a long-term clinical and patient reported outcomes on the use of the Gynecare TVT systems for SUI.[149] The first patient enrolled on February 16, 2007. However, because the TVT-S was losing market share and failing to meet expectations among surgeons, Ethicon discontinued the TVT World registry in March of 2009[150] stating that they "had sufficient data generated from 1,367 patients as of March 11, 2009 already enrolled . . . although we are still some way off the initial target of 5,000 patients."[151] TVT World closed 3,500 patients short of Ethicon's initial "class" goal because they determined that the TVT-S was not commercially viable.

Two KOL professors for Ethicon, Nilsson and Artibani, expressed worries about Ethicon "launching TVT Secur with no clinical data (other than the 50 patients, 5 weeks to follow up)."[152]Professor Artibani was "surprised Ethicon did not learn the lesson from the launch of a

[147] ETH.MESH.00371551.
[148] ETH.MESH.00409675.
[149] ETH.MESH.00134794 Slide 6.
[150] ETH.MESH.00134794 Slides 13 and 14.
[151] ETH.MESH.03208592.
[152] ETH.MESH.03172197.

prior product, MoniTorr…" when discussing the lack of clinical data. Harel Gadot, Ethicon's European Marketing Manager, then strongly recommended that Ethicon "find a way not to cancel completely the proposed RCT" because Ethicon assured their KOLs that they would conduct RCTs so that they would commit to being preceptors for the device. Because of this, Mr. Gadot encouraged Ethicon to protect Johnson & Johnson's reputation and not to cancel the RCT.[153] However, Ethicon elected to cancel the RCT anyway.

Carl Nilsson, the same Ethicon KOL who co-authored the 3, 5, 7, and 17-year studies on the TVT-Retropubic and was going to be Ethicon's "ambassador" for the TVT-S, wrote an article in 2015 related to the need for clinical studies on new medical devices.[154] While Dr. Nilsson did not specifically call out the TVT-S as being flawed, given the internal Ethicon documentation substantiating his criticisms of Ethicon with the device, it is particularly telling:

> Recent history includes the launch and withdrawal of many modifications and copies of the TVT procedure, which shows that any variation of a procedure needs its own thorough clinical testing before it can be accepted for common use. The surprisingly high rates of complications such as bladder perforation and post-operative voiding problems seen in more recent reports compared with the rates seen in the initial ones from the Nordic countries emphasizes the need for proper training and adherence to the standardized performance of the operation in order to avoid complications and poorer performance. It is a waste of both public and private resources to launch poorly documented new treatment concepts and it is especially wrong for the women suffering from [SUI] to become the subjects of experimental efforts without ethical approval and written informed consent.[155]

The long-term follow-up data (Ulmsten/Nilsson data) used by Ethicon to promote the lack of risk of TVT-S is spurious at best. We have incomplete data on the original cohort, data that is falsely reported, original sites that were excluded without explanation and a lead investigator who had a significant relationship and financial incentive to reach certain results

[153] *Id*.
[154] Nilsson, *Creating a gold standard surgical procedure: the development and implantation of TVT*, Int. Urogynecol. J. (2015) 26:467-269.
[155] *Id*.

with the data. This is the same data which is now used repeatedly in promotional and marketing materials sent to physicians.

I have reviewed over a thousand papers discussing, among other things, surgical methods, surgical techniques, complications, and summaries of clinical testing and trials on TVM products, including the TVT-S. I previously served on a medical advisory board where I helped design a RCT for a device used for the treatment of SUI. I have also acted as an investigator in conducting RCTs on drug treatments for urinary incontinence and phase 1 Federal trials on medical devices to seek clearance for over the counter use. Additionally, I have conducted RCTs on amnio-infusion and contraction stress tests during labor. I agree with Dr. Nilsson, along with Ethicon's other KOLs who advocated for Ethicon to conduct clinical testing prior to the commercialization of the TVT-S. Given both the completely different characteristics associated with this device and the unique surgical technique used to implant the TVT-S, for this product to be properly evaluated, the TVT-S and surgical procedures (associated with both the "U" and "hammock" placement) should have been used in short and long-term clinical studies to determine intraoperative/postoperative morbidity and surgical cure rates. In this respect, a carefully selected patient population with an extensive informed consent process designed to clearly notify participants that the use of the TVT-S was purely experimental in such studies would have been appropriate. If any such RCTs had been conducted, the various implantation issues and other flaws identified herein with the TVT-S would have been studied and identified prior to being permanently implanted into women's bodies. Instead, the TVT-S was introduced into the market place and sold as an "easy-fix" procedure to obstetric/gynecologists across the country, when only highly skilled pelvic floor surgeons should have implanted the TVT-S.

D. THE DESIGN OF THE TVT-S WAS DEFECTIVE.

Although Ethicon utilized the TVT and TVT-O as predicate devices in its TVT-S 510(k) application to the FDA, these devices are completely different from the TVT-S. For example, the TVT-S' inserters had never been used before[156] and the length of the tape and the mechanism of insertion are completely different. One of Ethicon's KOLs commented to an Ethicon employee in November 2007 that the "TVT S is so 'utterly different to the other TVTs that it probably shouldn't be called a TVT' and the speed to market and breadth of the launch did not take this into account."[157] Ethicon's World Wide Medical Director in 2007, Dr. David Robinson, recognized that the TVT-S was "a sling 'unto itself' as far as techniques go."[158]

The insertion mechanism was known to be difficult because of the complications with the dislodging of the anchoring of the TVT-S. There were also difficulties with the tape. It was very difficult to properly tension the device, and the need for significantly greater tension was never communicated to surgeons whose comments reflect the degree of tension. Thus, the low tension was proving quite difficult for surgeons than they were accustomed to seeing in the TVT or TVT-O, which resulted in lower cure rates.

Ethicon knew that the incision size was not accurate in the IFU and should have been wider. Ethicon also knew that the smaller incision size reflected in the IFU caused a greater risk of mesh extrusion/erosion to the patient. Internal Ethicon documents reflect there was no agreement on the amount of dissection or depth of the surgical incision with the TVT-S. The IFU states that the incision size should be 1.0-1.5 cm.[159] However, the "the

[156] Deposition of Dr. David Robinson, 7.24.13 Page 116 Lines 5-22.
[157] ETH.MESH.00327062.
[158] ETH.MESH.00642328.
[159] ETH.MESH.02340568-ETH.MESH.02340590.

cookbook," [160]"procedural pearls,"[161] and internal e-mails reflect the need for a larger incision size. On January 20, 2007,[162] Menachem Neuman (well-renowned urogynecologist from Israel and TVT-S trainer for Ethicon) wrote an email in response to Isabelle Perez's (Professional Education Co- Coordinator Ethicon France) request to share "success stories" from Neuman's recent TVT-S training visits to Portugal and other European countries during the last few months of 2006 and early January of 2007. Dr. Neuman related the following:

- It would be necessary for a surgeon in training to undergo 5 training operations with Neuman to become a "flying surgeon" (Preceptor). Thereafter, the "flying surgeon" would need an additional 20 to 30 operations to form the "inner-country" pyramid of homeland trainers.
- Surgeons who are more familiar with TVT-O will require more training for the TVT-S in order to overcome the "dragged bad habits" from the former operations to the new one. There are special differences between the TVT-O and TVT-S and those should be addressed to and respected if high cure rates and low complication rates are desired.[163]

In this email, Dr. Neuman attached a copy of his TVT-S Preceding Steps,[164] which do not parallel the TVT-S' IFU. But, Ethicon upper management was aware of this information because Dr. Neuman's email was forwarded to David Robinson, Kevin Mahar, Bob Roda (Ethicon Group Marketing Director Worldwide), and Dharini Amin (Ethicon Product Director) on January 23, 2007.

In February 2007, Dr. Robinson emailed a copy of an abstract prepared by Dr. Neuman to Judith Gauld.[165] The abstract evaluated Dr. Neuman's "learning curve" with his first 100 patients implanted with the TVT-S. The abstract concluded "[t]he trainer's learning curve was reasonable and yielded some insights, among them are the necessity of meticulous and proper

[160] ETH.MESH.03752501- ETH.MESH.03752506.
[161] ETH.MESH.07039973- ETH.MESH.07039975 (stating that the incision size should be 1.2-1.5 cm).
[162] ETH.MESH.02320485-ETH.MESH.02320489.
[163] ETH.MESH.02320486.
[164] ETH.MESH.02320488.
[165] ETH.MESH.01782942

dissection prior to tape placing and the need of applying some minimal extra tension on the mesh."[166] It noted that the TVT-S device "***being relatively slightly more rigid than the previous ones, tends to protrude the vaginal mucosa on the post-operative course***. This was addressed by abounding the rapidly absorbed vaginal stitches and by mucosal undermining in order to permit the tape to sink deeper, away from the vaginal mucosa. The inserters, being more than twice wider than the TVT and TVTO needles, necessitates larger tunnel; 12 mm's at least, in order to permit smooth passage of the tape and inserter and avoid mucosal placation which might lead to vaginal wall penetration."[167] In 2011, Dr. Neuman published his findings that the TVT-S caused significantly more dyspareunia than the TVT-O due the stiffness/rigidity of the mesh.[168]

On May 16, 2007, Harel Gadot wrote to several Ethicon employees, including Dr. Robinson, saying one of the main issues to be addressed in Ethicon's new procedural steps CD should be the "undermining" (as Dr. Neuman called it) to allow the mesh to lay flat under the urethra. All the surgeons felt that was a very important step that they were missing.[169] In reply to the email, Amin replied that "[a]ny changes will delay the project by 1 month and the US needs this soon before AMS launches [their mini-sling] at the end of June. If we need to change the video we can open another project for the European team to add additional footage to the current video."[170] In another reply, Amin wrote, "On the 1st page we added comment 'around 1.5 cm incision and of full thickness, to allow mesh to law flat underneath

[166] ETH.MESH.01782949
[167] ETH.MESH.01782956.
[168] Neuman M. Transobturator vs. Single-Incision Suburethral Mini-slings for Treatment of Female Stress Urinary Incontinence: Early Postoperative Pain and 3-year Follow Up. *J Min. Invas. Gynecol* 2011; 772 (dyspareunia rate over 162 patients with TVT-S 7.9% vs. TVT-O 0%, explaining dyspareunia due to rigidity and reduced flexibility of mesh with TVT-S because it was laser cut, which tends to result in stiff tape edges).
[169] ETH.MESH.03922436.
[170] ETH.MESH.03922435.

urethra. This may reduce risk of incision disruption and mesh exposure."[171] She also noted that "we cannot put pearls in the technical guide which is used to explain the IFU in detail."[172]

On July 26, 2007, Greg Prine (Regional Business Director - Sales) and Selena Lessa (Division Manager – Sales) received the Key Technical Points showing that the vaginal incision "should be made **slightly larger** than with conventional slings (**closer to 1.5 cm**) and of full thickness, to allow mesh to lie flat underneath urethra. This may reduce risk of incision disruption and mesh exposure."[173] In August 2007, Dr. Jaime Sepulveda, another Ethicon KOL, sent an e-mail with the summary of the "critical steps" session regarding the placement of the TVT-S. This email focused on the device placement, tensioning, inserter removal, and closure. On August 28, 2007, Mr. Prine received a copy of Dr. Sepulveda's summary of the Critical Steps session that was presented at an August 24th Ethicon meeting *with preceptors* (these are surgeons who are paid by Ethicon to train other surgeons on the TVT-S), where he wrote that "[a]n incision of 1.5 – 2.0 cm . . . was required."[174] In 2009, Dr. Sepulveda ran a training session where he noted that a vaginal incision of +/- 2 cm was *necessary* for the TVT-S.[175]

This disagreement over the incision size for the TVT-S was known and identified by Ethicon during the early stages of the TVT-S being on the market. Yet even though the IFU was the controlling document for surgeries, these subsequent "cookbooks" and "pearls" were only distributed to doctors if the representatives received complaints or were high volume users.[176]

---

[171] ETH.MESH.03922434.
[172] ETH.MESH. 03922435.
[173] ETH.MESH.17666960-ETH.MESH.17666969.
[174] ETH.MESH.10226089.
[175] ETH.MESH.02596703.
[176] ETH.MESH.03752501-ETH.MESH.03752506.

The TVT-S was also more prone to failing and maintaining the angle of correction at the urethra for control of SUI. The tensioning and fixation problems were known to Ethicon[177] as they saw inferior TVT-S cure rates as compared to the TVT and TVT-O.[178] Ethisorb may have also been a contributing factor to the fixation concern (it had never been studied for mesh fixation in the human pelvic floor region). One study showing a 42% failure rate with the TVT- S concluded that "[O]ur experience shows that despite its good short-term efficacy, TVT-Secur is associated with a high recurrence rate of SUI. Therefore, TVT-Secur does not seem appropriate for SUI first-line management in women."[179] In fact, Ethicon's internal documents showed that surgeons in 2007 were experiencing "high 'failure' rates across multiple centers."[180] Dr. Robinson was aware that possible complications associated with the TVT-S included multiple surgeries to treat the resulting erosion.[181] Studies revealed that women who received the TVT-S experienced higher rates of erosion and higher rates of reoperations because of the various defects noted herein. One study prepared by Lekha S. Hota, M.D., an Ethicon KOL, stated that "there also was an increased incidence of mesh exposure in the TVT-S group. Although the etiology of this complication is unclear, we theorize that the sharper edges of the TVT-S introducer potentially create more trauma to the vaginal epithelium and may result in high erosion rates."[182] Ethicon never investigated the possibility that its product's sharper edges might subject patients to greater tissue trauma,

[177] ETH.MESH.00329316, ETH.MESH.05473738, ETH.MESH.05530459, ETH.MESH.05530464, ETH.MESH.05530469.
[178] Hota L. TVT-Secur (Hammock) Versus TVT-Obturator: A Randomized Trial of Suburethral Sling Operative Procedures. *Female Pelvic Med Reconstr Surg.* 2012, 18(1): 41-45 (47% cure rate with TVT-S and 91% cure rate with TVT-0); Maslow K, Gupta C. Randomized clinical trial comparing TVT Secur system and trans vaginal obturator tape for the surgical management of stress urinary incontinence. *Int Urogynecol J* (2014) 25:909–914 (63% cure rate with TVT-S and 86% cure rate with TVT-O).
[179] Cornu JN, Midterm prospective evaluation of TVT-Secur reveals high failure rate, *Eur Urol.* 2010; 58(1):157-61.
[180] ETH.MESH.00642330- ETH.MESH.00642331.
[181] Depo of David Robinson, M.D 7.24.13 Page 355 Line 16 – Page 356 Line 8.
[182] ETH.MESH.04474756 – ETH.MESH.04474760.

potentially resulting in erosions.

Despite Ethicon's knowledge of these various defects, it kept the TVT-S on the market. Ethicon's Quality Board conducted an analysis due to complaints in Australia in 2007. At this time, they were told that the two most significant US complaints were that the implant pulls out with the inserter and that the inserter itself was difficult to remove.[183] A November 6, 2006 email from Mark Yale to Medical Director David Robinson[184] and others reveals an issue with the TVT-S arising shortly after the launch of the product (June 2006). The specific issue is regarding the withdrawal of device itself with inserter and anecdotal concerns of a high rate of occurrence with injuries related to device not coming off inserter during removal causing the device to be moved or pulled out along with inserter.

In a May 17, 2007 presentation to Ethicon employees by Dr. Axel Arnaud (Medical Affairs Director of Ethicon, Europe Middle East and Africa), he noted that "[s]ome key experts and non-experts are disappointed," and "[k]ey experts are abandoning the procedure." He went on to state that the "advantages of conventional TVTs are insufficient for accepting more failures."[185] On October 25, 2007, Dr. Aran Maree (Medical Director of Australia and New Zealand) attributed the failures to the product having been "launched as a substitute for TVT-O without enough clinical data to justify the roll-out," and that the original training program did not result in "competency in device insertion."[186] Furthermore, on November 2, 2007, Dr. Maree advised Catherine V. Beath (WW VP of Quality Assurance) that three seasoned surgeons experienced multiple 6-week failure rates—this included Prof. Malcolm Frazer, a surgeon who had performed about 700 TVT cases over the years, who experienced

[183] ETH.MESH.06051286 Page 5 and 25.
[184] ETH.MESH.0329316.
[185] ETH.MESH.00572598
[186] *Id*.

13 failures out of 20 surgeries (a 65% failure rate).[187] All of these surgeons determined that these failure rates that they were experiencing with the TVT-S were above their previous failure rates with the TVT and TVT-O. In 2014, the Cochrane Collaboration analyzed various single-incision operations for urinary incontinence in women by interpreting the results of a number of RCTs and quasi- RCTs.[188] Though there was no ultimate conclusion on the efficacy or safety of any SIS other than the TVT-S, SISs were noted to result in higher incontinence rates compared with inside-out transobturator slings (30% vs 11%; RR 2.55, 95% CI 1.93 to 3.36). The adverse event profile was also noted to be significantly worse, consisting of higher rates of operative blood loss, vaginal mesh exposure, and bladder/urethral erosion. These findings were mostly derived from trials involving the TVT-S. The authors concluded that the TVT-S was "considerably inferior to retropubic and inside-out transobturator slings" and was "inferior to standard mid-urethral slings for the treatment of women with stress incontinence." In fact, a systematic review of RCTs comparing single-incision mini-slings to standard midurethral slings needed to exclude data on the TVT-S in order to show there were no significant differences in efficacy or complication rates between mini-slings and midurethral slings.[189]

E. POST-MARKETING ADVERSE EVENTS

Ethicon did not actively try to determine how many patients were hurt by its devices,

[187] ETH.MESH.00312179-182

[188] Despite having already been withdrawn from clinical use at the time of the study, the report included the TVTSecur
"so that level 1a data" would be "available in the literature to confirm its lack of efficacy." Nambiar A, Single-incision sling operations for urinary incontinence in women; *Cochrane Database of Systematic Reviews* 2014, Issue 6.

[189] Mostafa A, Single-Incision Mini-Slings Versus Standard Midurethral Slings in Surgical Management of Female Stress Urinary Incontinence: An Updated Systematic Review and Meta-analysis of Effectiveness and Complications; *European Urology*, 2014; 402-427 ("This meta-analysis shows that, excluding TVT-Secur, there was no evidence of significant differences in patient-reported and objective cure between currently used SIMS and SMUS at midterm follow-up while associated with more favorable recovery time.").

including the TVT-S, or how severely they were hurt. Instead, Ethicon had a "passive" system of measuring how many and what type of adverse events the TVT-S was causing. Ethicon's Director of Post-Marketing Surveillance testified that this type of passive collecting of reports understates how many people are actually being hurt by its devices:

> THE WITNESS: So we -- from a reactive perspective for complaints, we can only process the complaints that are reported to us, so -- and as we discussed earlier, they come from many different avenues; but again, they're reactive in nature, which means we are processing what is given to us or reported to us.
> Q. You understand that spontaneous adverse event reporting, such as your department collects and analyzes, has been demonstrated to substantially under quantify the real complications in the world?
> A. So the adverse events that are reported to us, complications, complaints that are reported to us, are a subset of the events, complaints, complications that occur in the field.[190]

In fact, Ethicon employees ensured that they would not "actively" collect any complaints. When discussing how to perform a marketing survey with a number of physicians, Dan Smith wanted to ensure Ethicon people did not ask physicians questions that might "collect" a complaint:

> Just a thought with regard to us collecting information. Paul, what was the ruling from our compliance group regarding us asking questions/collecting data, did we have to log issues as complaints???? et cetera. If so, we should do this in a manner that avoids this issue.[191]

Dr. David Robinson, Ethicon's Medical Director, noted a reason that Ethicon might not want to actively collect adverse events about its products: "[I]f this starts getting reported, it is going to scare the daylights out of docs."[192]

---

[190] Lamont Dep. (4/4/13) 389:25-390:23; Yale Dep. (8/7/13) 126:20-127:7 ("So you would agree that generally in a passive complaint collection, which is what Ethicon had prior to this discussion about the registry, for example, in a passive collection, that it is well known and well recognized that adverse events are underreported. Correct? THE WITNESS: In general, the basic understanding in the world of complaints and adverse events is that you do not get 100 percent reporting, that, you know, it is not the perfect collection model to gather. So, yes, they are, in some manner, underreported.").

[191] ETH.MESH.01811770.

[192] ETH.MESH.00756984 (Email from David Robinson, M.D. to Giselle Bonet and Marty Weisberg).

Even though Ethicon limited its "surveillance" to passively collecting complaints, it did not do this well. For example, Mark Yale, the head of Ethicon's Worldwide Customer Quality team testified that all Ethicon employees had a legal duty to report any and all complaints to the Company about which they became aware.[193] When shown documentation, Yale admitted that this collection system was flawed. For example, employees in a US call center failed to report complaints,[194] employees in Eastern Europe did not know they were required to inform the Company of complaints and adverse events,[195] one Portuguese employee testified that he would not have reported the complaint, but someone had already informed the regulatory authorities:

> Q. So Francisco in Portugal working for Johnson & Johnson Medical says he wouldn't have reported this to you, this complication, except for the fact that somebody reported it to their regulatory authorities. Right?
> A. That's what he wrote. Correct.[196]

This line of questioning led to a consistent theme about adverse events and complications tracking at Ethicon – you don't know what you don't know. Yale testified:

> Q. So as you sit here today, you have no idea how many other complaints didn't make it here from Portugal, because Francisco Noronha from Johnson & Johnson decided that if it wasn't reported to his regulatory agency, he's not going to tell you about it. Right?
> THE WITNESS: I don't know what I don't know.[197]

When David Menneret, an employee of the mesh manufacturer at Ethicon SARL received a complaint about mesh being frayed (a significant issue as discussed above) he was unsure whether to report it as a "complaint" into the Ethicon complaint tracking system. He wrote:

[193] Yale Dep. (8-7-2013) 140:12 to 140:16.
[194] Yale Dep. (8-7-2013) 145:12 to 145:15.
[195] Yale Dep. (8-7-2013) 155:21 to 155:25.
[196] Yale Dep. (8-7-2013) 159:5 to 159:10.
[197] Yale Dep. (8-7-2013) 160:16 to 160:24.

> Please see attached below a letter...regarding Mesh fraying. I don't know exactly who should be informed of this kind of customer feeling so feel free to forward to anyone concerned. Do you think this should be entered as a complaint in the system?[198] Again, Yale testified that he could not know how many complaints went to the manufacturer about the fraying from the manufacturing process that ultimately were not reported to Ethicon's complaint tracking system.

He testified as follows:

> Q. You don't know how many times Menneret didn't report a complaint either. Right? You don't know what you don't know. Right?
> THE WITNESS: As I said before, I do not know what I do not know….[199]

Prior to March of 2006, Ethicon did not even have a formal procedure in place to capture adverse events from its own clinical trials. Therefore, they had no idea how many adverse events occurred but were not reported from those trials.[200]

In addition to the marketing materials, Ethicon also provided physicians with "Complications Statements" during training or upon request. These "Complication Statements" relied upon the information captured in Ethicon's complaint system – the same system described above. Accordingly, the capture of information for these statements was already severely compromised. However, even for those events Ethicon did capture, the reporting of these events in the Complications Statements was completely misleading.

Joseph Scavona, a complaint analyst, was responsible for creating one of these Complications Statements that was provided to physicians. He described how he created the statement and how, if a woman had multiple injuries, he only listed one injury on the chart. He wrote:

> [S]ome complaints could be described with multiple main & sub categories, but each complaint was only labeled with one of these categories (e.g. patient had pain, bleeding, hematoma, exposure, and dyspareunia thus complaint was

[198] ETH.MESH.01814252.
[199] Yale Dep. (8-7-2013) 168:24 to 169:12.
[200] Yale Dep. (8-7-2013) 194:22 to 195:7.

coded only "mesh exposure").[201]

This completely misrepresented the actual harms data. Moreover, the person making these decisions, Scavona, was not a medical doctor. He recognized these limitations and requested that medical review the complications data, but it did not occur.[202] Instead, physicians were provided with misleading, inaccurate and incomplete information in the Complications Statements.[203]

In my opinion Ethicon's collection and reporting of adverse events and complications to physicians and patients was incomplete, inaccurate and misleading. As manufacturers are the only entities with access to complaint information, physicians and patients must rely upon them to provide timely, accurate and complete information. Ethicon failed to do so. Without accurate information, physicians could not and cannot obtain informed consent from their patients, nor can patients give informed consent. Ethicon's complaint collecting and reporting system made this impossible.

E. ETHICON'S FAILURE TO DISCLOSE THE CONTENTS OF THE MSDS

According to Ethicon Medical Director, Dr. Martin Weisberg, a Material Safety Data Sheet (MSDS) is "a document that discusses the product, the composition, any potential hazards from it . . . Generally, the safety particular of products."[204] As it relates to polypropylene, I have reviewed several MSDSs for polypropylene resin used to manufacturer meshes used in various pelvic floor meshes. All of the MSDSs discussed below are available to the public.

Sunoco, the manufacturer for the polypropylene resin used to manufacture Ethicon's

[201] ETH.MESH.02122904 (Ex. 970) (Email from Joseph Scavona to others re "TVT Complications Statement 2008"). Complications Statement attached at ETH.MESH.00007091 at 2 (Ex. T-970).
[202] *Id.*
[203] Yale Dep. (8-8-2013) 294 to 300.
[204] Weisberg Dep. (8/9/13) 909:2-9.

pelvic floor products lists the possibility that polypropylene mesh can cause tumors or cancer. This is documented by the Sunoco MSDS[205] from April 13, 2005 which states in relevant part:

> OTHER INFORMATION
> Follow all MSDS/label precautions even after container is emptied because it may retain product residue.
> COMPONENT TOXICITY: Polypropylene has been tested in laboratory rats by subcutaneous implantation of discs or powder. Local sarcomas were induced at the implantation site. No epidemiological studies or case report suggest any
> chronic health hazard from long term exposure of polypropylene decomposition products below the irritation level. (OARC, 19, 128).[206]

Dr. Martin Weisberg, Ethicon Medical Director, is not only familiar with this MSDS, he also has personal experience with it. Dr. Weisberg agrees that the manufacturer of Ethicon's mesh did a study by implanting it under the skin of rats and it did in fact induce sarcomas.[207] Dr. Weisberg also agrees "if there was evidence of cancer-causing abilities of polypropylene . . . a reasonable doctor would want to know."[208] And, despite evidence to the contrary in the above MSDS for the resin used to make the polypropylene mesh for TVT, he is not aware of any instance when Ethicon "disclosed to any doctor that there's any evidence that the use of polypropylene mesh might induce sarcomas in its patients."[209]

Dr. David Robinson, a former Ethicon Medical Director, testified he was unaware of Ethicon ever performing any studies or research to determine whether polypropylene could cause cancer in the long term.[210] In addition, he testified that Ethicon never disclosed "the

[205] ETH.MESH.02026591 at 6591-6595.
[206] *Id.* at 02026595.
[207] Weisberg Dep. (8/9/13) 951:6-10.
[208] *Id.*
[209] Id. at 951:11-16.
[210] Robinson Dep. (9/11/13) 1105:17-110:14.

potential that polypropylene in the product could be cancer causing."[211] Dr. Robinson also testified that it would be reasonable for physicians to want to know about polypropylene possibly causing cancer.[212]

Another MSDS from Chevron Phillips,[213] a manufacturer of polypropylene resin states:

> MEDICAL APPLICATION CAUTION: Do not use this Chevron Phillips Chemical Company LP material in medical applications involving permanent implantation in the human body or permanent contact with internal body fluids or tissues.
> Do not use this Chevron Phillips Chemical Company LP material in medical applications involving brief or temporary implantation in the human body or
> contact with internal body fluids or tissues unless the material has been provided directly from Chevron Phillips Chemical Company LP under an agreement which expressly acknowledges the contemplated use.
> Chevron Phillips Chemical Company LP makes no representation, promise, express warranty or implied warranty concerning the suitability of this material for use in implantation in the human body or in contact with the internal body fluids or tissues.

With respect to the Chevron Phillips MSDS, Ethicon Medical Director, Dr. Martin Weisberg, testified that he did not have the Chevron Phillips MSDS in 2001 when he reviewed the Sunoco MSDS and no one at Ethicon alerted him to it.[214] If he had been alerted to the Chevron Phillips MSDS, it may have "triggered" an investigation on his part.[215] He also believes that if Ethicon knew about this MSDS, Ethicon should have studied the issue and, if they did not do so, it would have been a violation of the company Credo.[216]

Total Petrochemicals, the polypropylene resin manufacturer for the polypropylene used in AMS' pelvic floor products, Technical Data Sheet for Polypropylene PPR 7220, states in bold red lettering "Under no circumstances are any products sold by Total Petrochemicals

---

[211] Robinson Dep. (9/11/13) 1114:15-18.
[212] Robinson Dep. (9/11/13), 1115:5-19.
[213] Chevron Materials Safety Data Sheet Marlex Polypropylenes (All Grades) Revision Number: 3 (Ex. T-3137).
[214] Weisberg Dep. (8/9/13) 944:16-945:5.
[215] *Id.*
[216] *Id.* at 947:4-19.

suitable for human or animal implants." It is further documented that, "The above-mentioned product is NOT in compliance with the US pharmacopoeia because we DID NOT perform required tests." (emphasis from the original document).[217]

The manufacturer of the polypropylene resin for the polypropylene used in competitor pelvic floor products, Phillips Sumika Polypropylene Company, included a similar warning in its MSDS.[218] Specifically, it states:

> Do not use this Phillips Sumika Polypropylene Company material in medical applications involving permanent implantation in the human body or permanent contact with internal body fluids or tissues. Do not use Phillips Sumika Polypropylene Company material in medical applications involving brief or temporary implantation in the human body or contact with internal body fluids or tissues unless the material has been provided directly from Phillips Sumika Polypropylene Company under an agreement which expressly acknowledges the contemplated use. Phillips Sumika Polypropylene Company makes no representation, promise, express warranty or implied warranty concerning the suitability of this material for the use in implantation in the human body or contact with internal body fluids or tissues.

As discussed above, the possibility that polypropylene mesh can cause tumors or cancer is documented in the Sunoco MSDS, the manufacturer of the polypropylene resin used in the TVT Prolene mesh.[219] Specifically, the Sunoco MSDS from April 13, 2005 states:

> COMPONENT TOXICITY: Polypropylene has been tested in laboratory rats by subcutaneous implantation of discs or powder. Local sarcomas were induced at the implantation site. No epidemiological studies or case report suggest any chronic health hazard from long term exposure of polypropylene decomposition products below the irritation level."[220]

Despite this warning in the MSDS for the polypropylene resin used to manufacture the TVT mesh, there is no evidence that Ethicon informed surgeon about this important information contained in various Manufacturer Safety Data Sheets (MSDS) regarding the use

[217] ETH.MESH.02026591.
[218] Phillips Sumika Polypropylene Company Material Safety Data Sheet Marlex Polypropylene (All Grades) Revision Number: 5.03 Revision Date: 12/4/2008.
[219] ETH.MESH.02026591-6595.
[220] ETH.MESH.02026595.

of polypropylene. This information includes the dangers of using polypropylene in a permanent implanted medical device set forth in MSDS that were in the public domain and available to Ethicon if they chose to look. Ethicon also failed to inform physicians that laboratory studies on rats showed that polypropylene caused sarcomas.

The fact that this information has not been disclosed to physicians in any manner (IFUs, direct letters or promotional materials) is especially concerning in light of literature showing reports of cancer associated with polypropylene. Specifically, there have been cases of pseudotumor reported in polypropylene for hernia mesh[221] and inflammatory myofibroplastic tumor of low malignant potential with a TVT device.[222] In addition, there have been 2 cases of bowel cancer associated with mesh used for abdominal sacrocolpopexy, one associated with mersilene and one with polypropylene and TVT placement.[223] A case of primary vaginal leiomyosarcoma associated with TVT and anterior repair with Bard Duraderm has also been reported.[224]

Finally, a report of angiosarcoma associated with Darcon vascular grafts was reported in 1999.[225] The authors of this article noted at least 8 other sarcomas developing at the site of vascular prosthesis, and that the rate of these sarcoma, associated with foreign bodies, was much higher than the rate of sarcomas in general. All sarcomas associated with Dacron grafts were high grade histology and disseminated at the time of presentation. The authors also describe sarcoma reported at the site of other foreign bodies, such as shrapnel, bullets, steel plates and retained surgical sponges. They also note that the latency period from the acquisition of the foreign body and the development of sarcoma had a mean of 33 years. They

[221] Karrem, M., Community Oncology, Volume 7/Number 4/April 2010.
[222] Kwon S., et al, Female Pelvic Med Recontruct Surg, Volume 18, Number 4, July/August 2012.
[223] Ahuja, S., et al, Gynecol Surg 2011, 8:217-221.
[224] Moller, K., et al, Gynecologic Oncology 94 (2004) 840-842.
[225] Ben-Izhak, O., et al, Am J Surg Pathology, Issue: Volume 23 (11), 1999, p. 1418.

document that a chronic foreign body reaction, the same "microscopic foreign body reaction" described by Dr. David Robinson in his Sept 2013 deposition as being clinically insignificant, was the etiology of this carcinogenesis. The authors also describe sacromas developing in rodents after inert plastic polymers were placed in their soft tissue: "The sarcomas developed in rodents in which thick fibrous capsules developed around the implanted material." The authors conclude: "For unknown reasons, the cells in this inflammatory and repair process may undergo a malignant transformation, probably associated with oncogene activation and tumor suppressor gene inactivation. Further studies are warranted to search for the mechanisms involved in foreign body tumorgenesis." To date no manufacturer of mesh products has investigated this oncogenic potential as the authors recommended. In a report from the International Agency for Research on Cancer: Surgical Implants and Other Foreign Bodies, "When several polymers were tested in rats according to the same experimental protocol, sarcoma incidences ranged from 70% (polypropylene) to 7% (silicone)."[226] "Polymeric implants prepared as thin smooth films (with the exception of poly(glycolic acid)) are POSSIBLY CARGINOGENIC TO HUMANS."[227]

Given the fact that hernia mesh placement increased in the 1990's with the advent of laparoscopic placement, and that vaginal mesh placed for SUI and POP accelerated in the 2000's, we may be on the cusp of an ever increasing number of foreign body tumors associated with vaginal mesh. Ethicon did not undertake any long term testing to determine whether or not these warnings on the polypropylene resin manufacturers MSDS were associated with long term consequences for permanent human use. This is true despite the fact that Ethicon has knowledge of three of these cancer reports (Kwon, Moller and Ahuja) as they are referenced in

[226] International Agency for Research on Cancer, Summaries and Evaluations, Vol.:74 (1999).
[227] McGregor, D.B., et al, European Journal of Cancer 36 (2000) 307-313 (emphasis added).

Ethicon's 2013 Clinical Evaluation Report regarding TVT.[228]

Additionally, there is no evidence that Ethicon made any effort to inform surgeons of important information contained in various Manufacturer Safety Data Sheets (MSDS) regarding the use of polypropylene. This information includes the dangers of using polypropylene in a permanent implanted medical device. And, that laboratory studies on rats showed that polypropylene caused sarcomas in laboratory rats. Clearly, these facts are critical information relevant to both the surgeon evaluating his or her treatment options and to the patient's informed

consent decisions. As a result, Ethicon failed to act like a reasonable and prudent medical device manufacturer.

F. BENEFITS OF TVT-S OUTWEIGHED BY ITS COMPLICATIONS

It is my opinion, based on my training, experience and extensive review of the literature and Ethicon's internal documents that the benefits of the TVT-S are outweighed by the severe, debilitating and life changing complications associated with the medical device. It is clear that a substantial number of women who are implanted with the TVT-S have already and will continue to suffer chronic, debilitating erosions or pain, among other complications, and these life changing complications outweigh the benefits of the TVT-S, a device used to treat a quality of life issue.

This is especially true given that traditional surgeries like the Burch and pubovaginal slings are not associated with the frequency or extent of these life changing complications. The efficacy of the TVT-S is equivalent to the traditional surgeries like the Burch. Traditional surgeries are not associated with TVT-S mesh based complications like contraction and

[228] ETH.MESH.10150515.

erosion, but rather with clinically significant erosion. And, further, although traditional surgeries can cause symptoms such as pain following surgery, including dyspareunia, the risk, duration, extent and severity of chronic pain including dyspareunia following the TVT-S is much greater than with traditional surgeries, and of course those surgeries do not result in the often untreatable complications and symptoms that result from the TVT-S mesh.

There were reasonably feasible safer alternatives available to Ethicon for the treatment of patients. For example, the Burch procedure would have been an appropriate treatment for the stress urinary incontinence. The Burch procedure eliminates the risks specifically associated with the laser cut mesh used in the TVT-S because the Burch procedure does not require the use of mesh. Another feasible safer alternative to the TVT-S would have included autologous fascia slings. Sutures used in an alternative design to the TVT-S (i.e., Burch); an autologous fascial sling; or, an allograft sling (i.e., Repliform) would have been a safer alternative design to the TVT-S.

Moreover, because of the manufacturing and design defects present in the TVT-S, several additional feasible alternatives were available to Ethicon that would have been less dangerous. As I have testified in previous cases where women have suffered permanent debilitating injuries from TVT mesh products, these alternatives depend on the patient, patient's lifestyle, patient's medical history, and the injuries the patient suffers from. Stiff and Rigid mesh like the TVT-S mesh is especially prone to causing erosions, urinary dysfunction and pain, including pain with sex. Because of this, softer, lighter weight, larger pore mesh that is less stiff and implanted with a less invasive implantation method and with a more reliable method of securing the mesh in place would have been less dangerous and a feasible alternative. Eliminating the sharp introducer and defective fleece

tips and using as softer less stiff lighter weight mesh would have been safer. In addition, based on Ethicon's internal documents, deposition testimony, and the medical literature, Ethicon had lighter weight larger pore meshes that were less stiff and more compliant with patients' tissues that Ethicon marketed for use in the pelvis.

Unfortunately, although there have been a large number of studies and publications involving the TVT over the years, the quality of most of the studies is not good, and the amount of bias included in the studies and publications adds to the limited value that the studies offer about long term, severe and debilitating complications like chronic pain and erosions associated with the TVT-S. The 2011 Cochrane Collaboration (Ogah) concluded that most trials involving mid-urethral slings had short follow-up and the quality of evidence was variable such that the quality of evidence for the majority of trials was moderate with a minority having low-to- moderate evidence.[229] Few trials reported outcomes after 1 year and long term adverse effects had yet to be determined. There are only a handful of RCTs involving the TVT that are long term, and major and long term complications would unlikely be picked up in these RCTs in part because they are designed with a primary endpoint of efficacy, not safety. The true incidence are more likely to be determined by registries or databases, but published registries do not track certain complications such as pain or dyspareunia, and have not been designed to monitor long term problems (Tamussino, 2001 and 2007; Kuuva 2002, Collinet, 2008, Dykorn 2010). This void in studying and presenting the true incidence and nature of long term and life altering complications, along with the biases inherent in many of the studies, and other factors, negates the value of the large majority of the studies, and as a result, other sources of data such as published case series are relevant and

[229] Ohah, et. al., Minimally Invasive Synthetic Suburethral Sling Operations for Stress Unrinary Incontinence in Women: A Short Version Cochrane Review. Neurology and Urodynamics 30:284-291 (2011).

important to truly understand the nature of these complications. Ethicon's internal documents and data, which are not publically available, present a very different picture of the TVT-S than the information that has been shared with patients and physicians.

G. ETHICON PROVIDED INADEQUATE TRAINING FOR IMPLANTING THE TVT-S

Though internal documents reflected Ethicon was aware of the multitude of problems associated with the implantation of the TVT-S, Ethicon failed to offer adequate training/retraining to physicians and did not revise the IFU. Ethicon made no effort to market the TVT-S to the most skilled physicians, despite feedback from their own KOLs. Alternatively, Dan Smith, an engineer, was sent to train a number of surgeons around the world on how to correctly implant the TVT-S in addition to spearheading the direction of the product marketing. Internal Ethicon documents reflect knowledge of the inadequacy of its physician training as well as the deficiencies within the training programs.[230] On October 25, 2007, Dr. Aran Maree (Medical Director Australia/New Zealand) addressed the growing issue of failed TVT-S implants in Australia.[231] Based on information and different sources, Dr. Maree began inquiring into potential issues associated with the TVT-S in 2007. He noted the failure rates of three doctors in addition to Dr. Lucente's failure rates. Dr. Maree further stated he wasn't surprised at Dr. Lucente's rates as "[t]his is very different to the QA database numbers sent through from the 'reported' complaint rates by the USA sales earlier on."[232] At the end of October 2007, Dr. Maree placed a "quality block" on the TVT-S in Australia and

[230] ETH.MESH.0324086; *see also* ETH.MESH.0329557; *see also* ETH.MESH.00330141; *see also* ETH.MESH.03922618; *see also* ETH.MESH.02105223; *see also* ETH.MESH.00874445 Page 17.
[231] ETH.MESH.00642325 Page 6.
[232] ETH.MESH.03845446.

New Zealand, which prohibited the product from being released from the warehouse.[233] On November 1, 2007, the decision was made to withdraw the TVT-S entirely from the Australian market.[234] Subsequently, Dr. Maree emailed Catherine Beath stating: "We feel that withdrawing the product from the market here is currently the most appropriate action for Australia. We believe this to be appropriate until we are confident that a modified technique, appropriately documented and tested by way of clinical study, can be taught to our surgeons and will lead to optimal patient outcomes with this product."[235] A dear doctor letter was mailed in March 2008, explaining the concerns expressed by many surgeons.[236] As a result of this letter, surgeons stopped using the product and shipped their remaining stock back to Ethicon.[237]

Thus, in Australia, the first concern about the TVT-S was raised in approximately September 2007—by early November 2007, the product was no longer being sold.[238] No other countries were informed about the quality block or dear doctor letter in Australia.

Hi Aran

As discussed earlier today, below is a summary of the key reasons surgeons do not wish to be re-trained on TVT Secur a this point in time.

- lack of clinical evidence
- steep learning curve (ie Vince Lucentes data suggests the first 25 patients will have a high failure rate - surgeons aren't prepared to risk their patients)
- IFU versus "nuances" - very different
- Current data suggests success of 65-70% (Vince Lucente) which is significantly lower than the 85-90% proven success for TVT-O. Surgeons aren't willing to try new technology unless we are able to prove similar success rates via independent studies

239

[233] Dep. of Aran Maree 7.22.2013 at 189:14-190:22.
[234] ETH.MESH.00326842.
[235] ETH.MESH.00326842.
[236] ETH.MESH.05404976.
[237] Dep. of Aran Maree 7.22.13 at 265:4-18.
[238] Dep. of Aran Maree 7.22.13 at 271:14-22.
[239] ETH.MESH.00823421-ETH.MESH.00823422.

Ultimately, no Australian physicians elected to attend retraining on the TVT-S because they had no confidence in the device.[240]

The TVT-S required specialized training and Ethicon was aware of this need. Dr. Maree testified that the TVT-S was a product that had either a "substantially" new technique or significant modification from the predicate devices.[241] Ethicon should have, but failed to, provide adequate, mandatory follow-up training. Dr. Ramy A. Mahmoud (WW VP for Evidence Based Medicine and CEO at Ethicon from 2007 to 2010) testified that he recalled discussing with Dr. Robinson and other surgeons the importance of proper technique in implanting the TVT-S and "how important the training was in order to adopt the correct technique in order to achieve the desired success rate."[242]

In December 2006, Dr. Axel Arnaud (Medical Affairs Director of Ethicon, Europe Middle East and Africa) stated that even surgeons "who have been correctly trained and who have passed the learning phase, are raising concerns about the efficacy of the TVT Secur . . . They are asking for clear recommendations about the way to perform the procedure, in particular about the size of the dissection, the tension to be given to the tape and the way to perform a cough test,"[243] none of which were disclosed in the TVT-S IFU.[244] Dan Smith disagreed with Dr. Arnaud, finding Dr. Arnaud's suggestions (the "cook book") to be far too long with too much information in it. Dr. Arnaud emphasized that Ethicon could not "ignore that some surgeons who have been able in the past to successfully perform TVT and TVT-O are now struggling to achieve the same results with Secur." Dr. Arnaud continued that he

[240] ETH.MESH.04127331.
[241] Deposition of Aran Maree 7.22.13 Page 137 Line 8-16
[242] Deposition of Rahmy Mahmoud, MD 7.16.13 Page 380:5-10
[243] ETH.MESH.00519479
[244] ETH.MESH.02340568 (TVT-S IFU)

wished "the solution would just be to tell them to go back to their homework, but I am not sure it is the best one."[245] In the same internal communication, Dr. Robinson concluded that "it is just as clear that we are having some type of training problems and in order to prevent wide spread negative talk, I think we must take palliative steps quickly."[246]

A March 14, 2007 email sent by Dr. Robinson to Dr. Axel Arnaud acknowledged that Ethicon's first human use study taught "that the learning curve is longer than we thought, mesh tensioning is different than kits with sheaths and that following the IFU is important"[247] During a June 18, 2008 interview, KOL Carl Nilsson stated that the learning curve for him with the TVT- S was **"**100 patients before he was very good with very dry results."[248] Dr. Vincent Lucente, Ethicon Consultant and US KOL, had a 40% failure rate in first 25 patients, and 30% of his first 77 patients. Ethicon employees, including Dr. TC Khoo (VP of Strategic Medical Affairs for Asia Pacific) began to suspect that failed implantations were "related to operator based technique deployment."[249] Dr. Khoo sought to remedy any problems in training in order to "eliminate[ing] any possibility of product related issues while considering the adequacy of training and what is needed to properly rollout a device" so that patients do not get "the short end of the stick."[250] Dr. Khoo found the "responsibility of controlling the adequacy of training is critical."[251]

Around October 2007, Dr. Maree expressed his concerns that the "current training program may not result in competency in device insertion or result in clinical efficacy. There appear to be 'tricks' to insertion of the product and removal of the inserters which prevent

[245] ETH.MESH.01784428, Page 2 and 3
[246] ETH.MESH.01784428, Page 1
[247] ETH.MESH.03922618
[248] ETH.MESH.04048515 at 3.
[249] ETH.MESH.00642325 Page 3
[250] *Id.*
[251] *Id.*

dislodging the device in the process."[252] As Dr. Maree clearly stated to Ethicon, "the average practitioner finds it too complicated to insert correctly and cannot master the process."[253] Because of the difficulty of inserting the product and the inadequate training, which left surgeons unable to achieve competency in insertion, Dr. Maree recommended "restrict[ing] access to those who can."[254] An Ethicon memo regarding TVT-S by Mr. Smith noted the "implications" of achieving competency on the TVT-S: "extensive training requirements, possible loss of market share."[255] Despite complaints from its own KOLs, Ethicon "rushed" the TVT-S to market, marketed it to all surgeons (even though the most experienced surgeons were experiencing difficulties obtaining successful results with the device), and failed to ever restrict access to this device.

V. CONCLUSION

Ethicon marketed and sold the TVT-S despite the fact that it had numerous characteristics making it unsuitable and not reasonably safe for implantation in a woman's vagina. Among other noted herein, these characteristics include the following: (1) excessive rigidity; (2) degradation of the mesh; (3) chronic foreign body reaction; (4) infections and bio-films; (5) fibrotic bridging leading to scar plate formation and mesh encapsulation; (6) shrinkage/contraction of the encapsulated mesh and (7) stiffness and rigidity.

Regardless of skill level, there were numerous known risks by Ethicon that were undisclosed in the TVT-S' IFU. Not only did Ethicon sell a product which should never be put in the vagina, it failed to inform physicians and their patients about numerous risks associated with the product despite the fact that these risks were known before the product was

[252] ETH.MESH.00642330- ETH.MESH.00642331.
[253] ETH.MESH.00642327.
[254] *Id*.
[255] ETH.MESH.00858636-639 ("Do not underestimate the learning curve for a device which seems simple").

launched. The IFU warnings that were provided were wholly inadequate and, coupled with the device's various defects, demonstrate the TVT-S was unreasonably dangerous as sold. Ethicon has removed the ability of physicians to appropriately inform their patients of the risks and benefits of the TVT-S and made it impossible for women to consent to the procedure. In addition, despite having knowledge to the contrary, Ethicon never informed physicians and their patients that the TVT-S was associated with cancer and could be toxic to their bodies. Finally, while keeping this information from women, Ethicon marketed its product with promotional pieces that did not disclose key conflict of interest information or the true complication rates of its products.

As a result of these failures, the TVT-S has caused and will continue to cause a multitude of injuries in women, including the potential for multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, nerve injury, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others.

All opinions I have are to a reasonable degree of medical certainty. I incorporate my past reports and testimony on the Secur device and the laser cut mesh used herein. I reserve my right to amend my opinions if further information is provided in any form including, but not limited to, corporate documents, depositions and expert reports of both Plaintiff and Defense experts.

Date of Report: May 22, 2017

Sincerely,

Bruce Rosenzweig, M.D.